molecules

MDPI

Review

Hunting Bioactive Molecules from the *Agave* Genus: An Update on Extraction and Biological Potential

Misael Bermúdez-Bazán [1], Gustavo Adolfo Castillo-Herrera [1], Judith Esmeralda Urias-Silvas [1], Antonio Escobedo-Reyes [2] and Mirna Estarrón-Espinosa [1,*]

[1] Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco, A.C., Unidad de Tecnología Alimentaria, Camino Arenero 1227, El Bajío, Zapopan 45019, Mexico; mibermudez_al@ciatej.edu.mx (M.B.-B.); gcastillo@ciatej.mx (G.A.C.-H.); jurias@ciatej.mx (J.E.U.-S.)

[2] Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco, A.C., Unidad de Servicios Analíticos y Metrológicos, Av. Normalistas No. 800, Guadalajara 44270, Mexico; aescobedo@ciatej.mx

* Correspondence: mestarron@ciatej.mx; Tel.: +33-334-552-00 (ext. 1940)

Abstract: Agaves are plants used in the production of alcoholic beverages and fibers. Ever since ancient times, pre-Hispanic cultures in Mexico have used them in traditional medicine to cure different ailments. Over the years, studies of the active principles responsible for the therapeutic benefits of agaves have increased. Leaves and fibers are the main agro-wastes generated in tequila and mezcal production, while fibers are the main waste product in the textile sector. Different investigations have referred to the agro-waste from agave processing as a source of bioactive molecules called secondary metabolites (SM). Among them, phenols, flavonoids, phytosterols, and saponins have been extracted, identified, and isolated from these plants. The role of these molecules in pest control and the prospect of metabolites with the biological potential to develop novel drugs for chronic and acute diseases represent new opportunities to add value to these agro-wastes. This review aims to update the biological activities and recent applications of the secondary metabolites of the genus *Agave*.

Keywords: secondary metabolites; bioactive compounds; agave agro-wastes; biological activity

Citation: Bermúdez-Bazán, M.; Castillo-Herrera, G.A.; Urias-Silvas, J.E.; Escobedo-Reyes, A.; Estarrón-Espinosa, M. Hunting Bioactive Molecules from the *Agave* Genus: An Update on Extraction and Biological Potential. *Molecules* **2021**, *26*, 6789. https://doi.org/10.3390/molecules26226789

Academic Editors: Giuseppe Antonio Malfa, Rosaria Acquaviva and Maria Fernanda Taviano

Received: 11 October 2021
Accepted: 5 November 2021
Published: 10 November 2021

1. Introduction

The agaves are perennial plants that use Crassulacean Acid Metabolism (CAM), which allows their adaptation to arid weather ecosystems [1]. The *Agave* genus is the largest of nine subgenres of the *Asparagaceae* family, with 210 species, of which 119 are endemic in Mexico; thus, it is considered the center of diversity of these plants [2,3]. Geographically, it is distributed within an area stretching from the southern United States to Ecuador [2].

The production of alcoholic beverages such as tequila, mezcal, and bacanora represents the most traditional use of these plants [4]. Nevertheless, the high demand for these products has led to the production of different agro-wastes that contaminate with the potential of being dangerous for the environment. Between 2015 and 2019, 1.434 billion liters of tequila were produced, which created an estimated 5,168,200 tons of agave leaves in waste. While the mezcal industry reportedly produced 27,663,459 liters, no official data regarding agro-waste generation of this beverage exist [5].

In the textile industry, obtaining fibers from *Agave lechuguilla* Torr. leaves is an important economic activity in this sector in Mexico. Within Mexico, the states of San Luis Potosí, Coahuila, Nuevo León, Zacatecas, Durango, and Tamaulipas are the main producers of this raw material, from which only 15% is product and 85% is an agro-waste called "guishe". This industry generated 150 tons of guishe per year [6–8]. Agro-waste production in the form of leaves and fibers has become an environmental concern.

Agave in Traditional Medicine

In ancient times, pre-Hispanic cultures in Mexico such as the Mayans and the Aztecs used agaves for medicinal purposes because of their therapeutic properties [9,10]. For example, the Mayans obtained leaf juice from the *A. fourcroydes* Lem. to heal wounds via topical application. In contrast, the roots and leaves of *A. angustifolia* Haw. were used to treat cutaneous and excretory skin infections and treat snakebite [11].

The Aztecs squeezed the fresh leaves of *A. atrovirens*, *A. americana*, and *A. potatorum* Zucc. to obtain concentrated sap. Later, they mixed it with hot urine, salt, honey, and some other medicinal plants. Other preparations involved *Comelina pallida* as a hemostatic agent. Finally, the mixture was applied to deep wounds [12].

The Tarahumara indigenous culture from Chihuahua domesticated a few *Agave* species and used these plants in medicinal preparations that consisted of applying leaf juice to festering sores. The sap was used to treat ocular infections, while other preparations with whole leaves were used to cure headaches [13].

Worldwide, different indigenous cultures have used these plants for their therapeutic effects. They have employed some species in the treatment of insect-borne diseases [14], rheumatic inflammatory affections [15], and nervous system diseases such as meningitis and sciatica [16]. Other medicinal preparations were preserved over the years, for example, the remedies prepared from *A. angustifolia* Haw., described by García Mendoza et al. [17]. This and other medicinal uses of different *Agave* species are summarized in Table 1.

Table 1. Medicinal uses of the *Agave* genus.

Species/Tissue	Medicinal Use	References
A. potatorum Zucc./leaf	Healing and cicatrization of wounds Infusions to heal respiratory infections	[18]
A. americana L./leaf, roots	Healing and cicatrization of wounds from leaf gel Syphilis treatment, anesthetic, headache, rheumatic pain, and broken bones Treatment of gout disease, infections, and burns	[19] [15] [20]
A. sisalana/leaf	Treatment for tick-borne diseases Stomach detoxifier and constipation Antimicrobial against pathogen biota of the intestines and stomach	[14] [21] [22]
A. sisalana/roots	Antidiarrheic	[23]
A. sisalana/leaf *A. karattos* Linnaeous/leaf	Treatment against meningitis and sciatica	[16]
A. angustifolia Haw./leaf, roots, fibers, leaf juice and root	Skin eruptions, kidney disease, and hepatic affections. It has antiparasitic and anti-hemorrhagic qualities	[17]

Until now, the medicinal applications of agave plant constituents were the prelude to many research studies conducted to discover the bioactive compounds responsible for their biological activity by applying different extraction technologies and analytical tools.

This review aims to describe various recent studies on secondary metabolites that have been extracted, isolated, and identified in different *Agave* species. It also describes those studies that have examined the bioactive properties of specific molecules and the biological activities of crude extracts with potential applications.

2. Extraction Methods Used to Recover Polyphenolic Compounds from *Agave* Agro-Waste

A previous review by Almaraz et al. [24] described the phenolic compounds of agaves. This section updates the information on the extraction and identification of different polyphenolic compounds and the factors that influence their extraction and occurrence in the *Agave* genus.

Phenolic compounds are polar molecules that possess an aromatic benzene ring, substituted with one or more hydroxyl (-OH) groups while flavonoids have more than one

phenyl ring. Their structure has a heterocyclic ring of benze-γ-pyrane, which is hydroxylated in distinct patterns [25]. Both types of metabolites can be methylated, glycosylated, and acylated. These structural modifications have been attributed to biochemical reactions of the vegetal metabolism and they impact the biological activity [26].

Because of the high polarity of glycosylated polyphenols, aqueous mixtures with a polar organic solvent have been employed to maximize their recovery. Barriada-Bernal et al. [27] used two extraction stages with 60% and 30% (*v*/*v*) ethanol, respectively, on *A. durangensis* Gentry flowers, and were able to identify through HPLC-UV-VIS, quercetin-3-*O*-[rhamnosyl-(1→6)-galactoside], kaempferol-3-*O*-[rhamnosyl-(1→6)-glycoside], kaempferol-3,7-*O*-diglycoside, and quercetin-3-*O*-glycoside as the most abundant molecules. Similarly, Almaraz-Abarca et al. [28] employed 60% (*v*/*v*) methanol on *A. victoriae-reginae*, *A. striata* Zucc., and *A. lechuguilla* Torr. leaves. They identified 25 glycosylated flavonoids and high levels of 3-*O*-glycosides of kaempferol were reported in these species. Besides, the presence of the glycosides of isorhamnetin, quercetin, and herbacetin were also reported.

Morreeuw, Escobedo-Fregoso, et al. [29] investigated the effect of binary aqueous mixtures solvents of *A. lechuguilla* Torr. leaves, and found that an ethanol–water mixture of 70:30 (*v*/*v*) enhanced the recovered yields of cyanidin and delphinidin. Conversely, an aqueous methanol mixture 60:40 (*v*/*v*) resulted in a more suitable extract for flavonoids due to its high polarity, and it obtained the highest yields of isorhamnetin and hesperidin.

Later, Morreeuw, Castillo-Quiroz, et al. [30] confirmed with HPLC-MS/MS that the hydroalcoholic mixture 70:30 (*v*/*v*) of *A. lechuguilla* Torr. was plentiful in mono-, di- and triglycosylated derivatives of apigenin, isorhamnetin, quercetin, and anthocyanins. Additionally, it was observed that the presence of more than one glycoside moiety was influenced by regional factors. Therefore, those extracts that belonged to drought regions accumulated -di or -tri glycosylated flavonoids; these compounds can provide better tolerance to drought stress [30]. Other studies on other *Agave* species demonstrated that drought stress induced an increase in these compounds and other secondary metabolites [31,32].

Morán-Velázquez et al. [33] investigated the use of accelerated solvent extraction as applied to young leaf spines of *A. fourcroydes* Lem. The extracts were plentiful in proanthocyanidins; this was confirmed by UHPLC-MS/MS. The accumulation of these metabolites into the fiber of young spines was possibly due to the laccase enzyme activity implied in the proanthocyanindins biosynthesis pathway. The authors associated this finding with the high abundance of (+)-catechin, (−)-epicatechin, and their glycosylated derivatives, as well as flavonoids which are the precursors of these compounds. Iser et al. [34] found the presence of tannins, phenols, and flavonoids in ethanolic and aqueous extracts from stems of this species.

In general, the variation in the total phenolic and flavonoid contents and other secondary metabolites has been described in relation to the type of *Agave* species, plant age, geographical origin, and solvent [35–40]. Ben Hamissa et al. [41] showed that high temperatures and pressures also improved the yield of phenols and flavonoids. Furthermore, emerging extraction processes such as ultrasound-assisted extraction also enhanced the yield of these compounds and reduced extraction times [42].

Pretreatments prior to the process and extraction type also influence the nature of the recovery of polyphenols from agaves. Contreras-Hernández et al. [43] found through HPLC-MS/MS that the phenolic composition of acetone extracts (85% *v*/*v*) from leaves of *A. durangensis* Gentry pretreated at a temperature of 120 °C and separately with an ultrasound had different phenolic profiles. Higher temperatures led to the partial degradation of lignin and the chemical conversion into new phenol molecules. Alternatively, the ultrasound-assisted extraction increased the content of specific flavonoids, such as quercetin, rutin, procyanidin B2, and others. Cavitation phenomena promote the rupture of the vacuoles, which leads to the release of aglycones from these compounds and consequently increases the yield of the recovered phenols [44].

A study reported by Avila-Gaxiola et al. [45] proved that a temperature of 100 °C applied in the pretreatment stage did not degrade the recovered phenolic acids of an

aqueous extract of *A. tequilana* Weber. The thermal pretreatment promoted the generation of new phenolic compounds, such as 4-hydroxy-benzoic acid, pyrocatechol, acetovanillin, vanillin, and 2-furoic acid.

Because agave extracts are susceptible to undesirable degradation reactions by biologic contamination or high temperatures involved in their pre-processing, the stability and bioactivity of polyphenols and other secondary metabolites might be compromised. To overcome this, Santana-Jiménez et al. [46] found that the irradiation by UV-C light at doses of 10.93 mJ/cm^2 for 30 seconds inactivated the native microbiota from piña crude extracts of *A. tequilana* Weber and did not affect the antioxidant or extract color. In this way, the irradiation by UV-C light for short times may represent a suitable technology to preserve agave crude extracts.

Acid hydrolysis is another pretreatment used in the extraction of phenolic compounds. One study reported an increase in the yield of these compounds in hydrolyzed extracts of *A. lechuguilla* Torr. The extracts showed aglycones and dimeric flavonoids, such as quercetin-4β-afzelechin [47]. Contrary to these results, Mitchell et al. [48] reported trace amounts of phenolic acids in hydrolyzed leaf extracts of *A. americana*, *A. fourcroydes*, and *A. tequilana*, respectively.

3. Bioactivity of Identified Phytochemicals from the *Agave* Genus

This section focuses on the description of the biological activities of identified and isolated polar and non-polar compounds to show the potential of novel bioactive molecules that were found in the literature related to the *Agave* genus. This information is summarized in Table 2.

Table 2. Biological activity of identified/isolated phytochemicals from the *Agave* genus.

Specie/Tissue	Compound(s)	Biological Activity	Dose	Study Model	References
		Phenolic Compounds			
A. durangensis Gentry Leaf	Flavonoid glycosides, aglycones, phenolic acids, proanthocyanins	Stimulant expression of enzymes	-	*N. crassa* ITD-G7 *A. niger* ITD-G1	[43]
A. lechuguilla Torr. Leaf	Afzlequin-4-β-quercetin; dimeric flavonoids, quercetin, kaempferol	Anticancer	IC_{50}: 6.96 µg/mL	SK-LU-1 cells	[47]
A. americana L. Leaf	Flavonoid glycosides of kaempferol, quercetin, isorhamnetin, ellagic acid hexoside	Insecticide Anti-repellent	10.55 µg/insect RD: 0.055 µg/cm^2	*Sytophilus oryzae*	[49]
A. lechuguilla Leaf	2,4,6-trinitrophnol, flavonoids, carboxylic acids, 2-aminomethil-propanol	Insecticide	LD_{50}: 1035 mg/mL	*Bemisia tabaci*	[50]
A. pygmaea Gentry *A. angustifolia* Haw. cv. *marginata* Leaf	Phenolic acids, flavonoid glycosides, homoisoflavonoids	Anti-inflammatory Anti-ulcerogenic	200 mg/kg 20 mg/kg	Wistar rats: rat paw stomach	[51]
A. americana L. Leaf	Apigenin	Antifungal	IC_{50}: 72.15; 18.83 µM	*A. oryzae* α-amylase	[52]
A. americana L. Leaf	p-coumaric acid, puerarin	Antidiabetic	IC_{50}: 98.8 µM, 3.87 µM	Human α-amylase	[53]
A. sisalana Fiber	Acylated glycosyl flavonoids, flavonoid glycosides, phenolic acids	Stimulant and growth protection of microgreens	-	Microgreens	[54]

Table 2. *Cont.*

Specie/Tissue	Compound(s)	Biological Activity	Dose	Study Model	References
		Saponins			
A. salmiana Sap	Kammogenin-pentaglucoside and tetraglycoside, Gentrogenin pentaglucoside	Anticancer	IC_{50} 82.7, 108.4 µg/mL	HT-29 cells	[55]
A. americana L. *marginata* Hort. Leaf	Cantala-saponin-1	Anti-neuroinflammatory	5-10 mg/kg	Rat brain	[56]
A. salmiana Sap	Kammogenin-glycosides	Anticancer	50 µg/mL	Hep-G2, CaCo-2 cells	[57]
A. marmorata Roezl. Leaf	Smilagenin-diglycoside	Immunomodulatory Anti-inflammatory	IC_{50}: 50 mg/mL, 0.086 mg/mL	RAW 264.7 cells	[58]
A. sisalana Perrine Leaf juice	Glycosylated steroidal saponins Hecogenin-pentaglycoside	Cytotoxic	IC_{50}: 125 µg/mL	C6 cells	[59]
A. sisalana Perrine Leaf juice	Steroidal saponins	Antineoplastic	50 µg/mL	Vero-cells Human lymphocytes, rats	[60]
A. angustifolia var. *marginata* Leaf	Steroidal-hexaglycosylated saponin	Anti-ulcerogenic	100 mg/kg	Rat stomach	[61]
A. seemanniana Jacobi Leaf	Steroidal saponins	Analgesic Anti-inflammatory Anti-ulcerogenic	100 mg/kg	Rat stomach	[62]
		Phytosterols			
A. tequilana Weber Piña	β-sitosterol-glycoside, stigmasta-3,5-dien-7-one Cicloartenone, cycloartenol	Immunomodulatory Anti-inflammatory	50 mg/kg	Urine, blood serum, kidney rat	[63]
A. angustifolia Haw. Leaf	3-*O*-[(6′-*O*-palmitoyl)-β-D-glucopiranosyl-sitosterol]	Immunomodulatory Anti-inflammatory	50 mg/kg	Mice ear edema	[64]

RD: repellent dose, IC_{50}: Half maximal inhibitory concentration, LD_{50}: Median lethal dose.

3.1. Polar Compounds: Phenols and Flavonoids

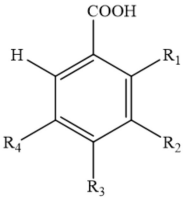
The biological potential of polyphenols from different *Agave* species has been studied and assessed in vivo. The hydroalcoholic extract of *A. lechuguilla* showed insecticide activity against *Bemicia tabaci* at LD_{50}: 1057 mg/L after 72 h, no positive control was used [50]. Another study reported the insecticide activity of aqueous methanol extracts on *Sitophylus oryzae*, at LD_{50}: 10.55 µg/insect after 72 h vs. malathion at LD_{50}: 2.34 µg/insect after 24 h [49]. Interestingly, an *A. americana* L. extract exerted repellent activity at RC_{50}: 0.055 µg/cm^2 while malathion did not present this activity. Besides, the chemical profile of *A. americana* L. presented flavonoids such as quercetin, isorhamnetin, kaempferol, and their glycosylated derivates and an ellagic acid glycoside was also identified, with the repellent activity associated to these compounds [49].

The anti-inflammatory and immunomodulatory activity of leaf extracts from *A. desmettiana* Jacobi, *A. angustifolia* Haw. cv. *marginata*, *A. americana* L., *A. americana marginata* Trel, and *A. pygmaea* Gentry were studied by El-Hawary et al. [51]. In contrast, *A. pygmaea* Gentry and *A. angustifolia* Haw. cv. *marginata* exerted the highest immunomodulatory activity at a concentration of 200 mg/kg on in vivo inflammation models and decreased the concentration levels of pro-inflammatory cytokines, which were different and lower than indomethacin administration. Alternatively, the production of IL-10 cytokine increased, which promoted an anti-inflammatory effect. Overall, these species showed different phenolic acids, glycosylated flavonoids, and homoisoflavonoids in their metabolomic profile, such as fukiic acid, sinapic acid, psicidic acid, methyl gallate, rutin, kaempferol, quercetin glucosides, eucomol, and dyhydroeucomin, and its occurrence was associated with such effects.

Anticancer activity has also been seen against lung cancer cell-lines in ethanolic leaf extracts from *A. lechuguilla* Torr. The crude extracts showed 75.7% of cellular growth inhibition in SK-LU-1 cells at IC_{50} 50 µg/mL vs. the anticancer drug Paclitacxel used as a positive control with 1.2% at 5 µg/mL. However, fractionated extracts presented this effect at a minor concentration (IC_{50}: 6.96 µg/mL) due to the elimination of residual sugars from extracts that are the substrates of these cell lines. These findings indicated that residual sugars in crude extracts attenuated the biological activity [47].

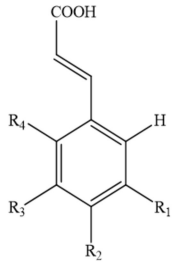
Both antifungal and antidiabetic properties were reportedly seen in *A. americana* L. leaf extracts. Two studies found that the bioactive potential is selective and depends on the nature of the isolated molecule. Puerarin and apigenin isolated from this species showed greater inhibitory effects against *A. oryzae* α-amylase, while p-coumaric acid proved a major inhibitor to human α-amylase at IC_{50}: 98.8 µM, with an inhibition rate 2.3 times higher than acarbose. Thus, isolated flavonoids may be used as therapeutic agents for postprandial glycemia [52,53].

Contreras-Hernández et al. [43] confirmed that the presence of phenolic compounds that were identified in *A. duragensis* Gentry leaves enabled the production of industrial enzymes during fermentation with *A. oryzae* and *N. crassa*. Another study of this species reported that fibers worked as a growth medium for microgreens because of the presence of phenolic acids and glycosylated flavonoids, which adopted a protector role during their development [54]. Some of these compounds include the glycosides and acyl glycosides of kaempferol and quercetin and novel phenolic acids (illustrated in Figures 1–3).



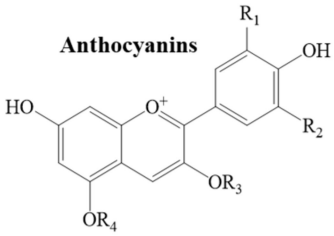
Hydroxybenzoic acids

	R1	R2	R3	R4	mg/L	Detection method
3,4-Hydroxybenzoic acid	H	H	OH	OH	-	HPLC-MS/MS [43]
4-Hydroxybenzoic acid	H	H	OH	H	86.8± 3.8	HPLC[45], FTIR [45]
Acetovanillin	H	OCH_3	OH	H	1.9 ± 0.3	HPLC[45], FTIR [45]
Gallic acid	H	OH	OH	OH	-	
Salicylic acid	OH	H	H	H	-	HPLC-MS/MS [43]
Vanillic acid	H	OCH_3	OH	H	-	
Vanillin	H	OCH_3	OH	H	27.1	HPLC[45], FTIR [45]



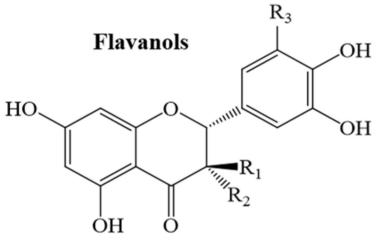
Hydroxycinnamic acids

	R1	R2	R3	R4	R5	µg/g DW	Detection method
Chlorogenic acid	OH	OH	H	H	QA	9947 ± 1095	
Caffeic acid	OH	OH	H	H	H	48.79 ± 7.2	UHPLC-MS/MS [54]
Caffeic hexoside	O-glc	OH	H	H	H	55.07 ± 8.1	
4-Caffeoyl-quinic	OH	OH	H	H	QA	-	HPLC-MS/MS [43]
3,4 Dicaffeoyl-quinic acid	OH	OH	H	H	QA	23.75 ± 1.39	
Ferulic acid	H	OH	H	H	-	20.12 ± 0.11	UHPLC-MS/MS [54]
Feruloyl-quinic acid	H	OH	H	H	QA	281.26 ± 54.2	
Feruloyl-glycoside	H	OH	H	H	O-glc	84.61 ± 4.6	
p-Coumaric acid	H	OH	H	H	-	-	HPLC-DAD [53]
p-Coumaroyl-quinic acid	H	OH	H	H	QA	40.40 ± 4.78	UHPLC-MS/MS [54]
Rosmarinic acid	OH	OH	H	H	DHLA	20.52 ± 0.07	
Sinapic acid	H	OCH_3	OH	OCH_3	-	-	HPLC-MS/MS [43]
Transcinnamic acid	H	H	H	H	-	-	

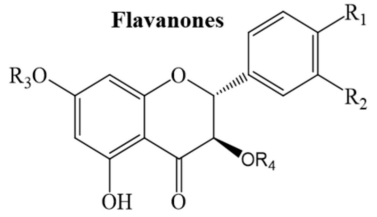


	R1	R2	R3	R4	µg/g DW	Detection Method
Cyanidin	OH	OH	H	OH	12.32	HPLC-UV-MS [29]
Cyanidin-3-O-glucoside	OH	H	glc	OH	-	
Cyanidin-3-O-rutinoside	H	OH	O-rut	OH	-	HPLC-MS/MS [29]
Cyanidin-3,5-O-diglucoside	OH	OH	O-glc	O-glc	-	
Delphinidin	OH	OH	H	OH	24.23	HPLC-UV-MS [29]
Delphinidin-3-O-glucoside	OH	OH	glc	OH	-	HPLC-MS/MS [29]
Gentiodelphine	OH	O-CA-glc	O-glc	O-CA-glc	-	

Figure 1. *Cont.*



	R1	R2	R3	µg/g DW	Detection Method
Dihydromyricetin	OH	H	OH	-	HPLC-MS/MS [29]
Dihydroquercetin	OH	H	H	-	
(+)-catechin	OH	H	H	7.91	HPLC-UV-MS [29]
(-) -epicatechin	H	OH	H	-	UHPLC-MS/MS [33]
Gallocatechin	OH	H	OH	-	HPLC-MS/MS [43]
Epigallocatechin	H	OH	OH	-	
Epicatechin gallate	H	O-GA	H	-	HPLC-MS/MS [43]
Gallocatechin gallate	H	O-GA	OH	-	



	R1	R2	R3	R4	µg/g DW	Detection Method
Hesperidin	OH	OCH_3	H	O-rut	32.90 ± 4.54	HPLC-UV-MS [30]
Hesperidin-methylchalcone	OH	OCH_3	H	O-rut		HPLC-MS/MS [29]
Naringin	H	OH	H	O-rut		
Naringenin	H	OH	H	H	1.43 ± 0.07	HPLC-UV-MS [30]
Naringenin-7-O-rutinoside	H	OH	H	O-rut	-	HPLC-MS/MS [29]

Figure 1. Current phenolic acids and flavonoids identified and quantified in the *Agave* genus, CA = cafeic acid, GA = gallic acid, rut = rutinoside, glc = glucoside, QA: quinic acid, DHLA= 3,4-dihydroxiphenillactic acid [29,30,33,43,52–54].

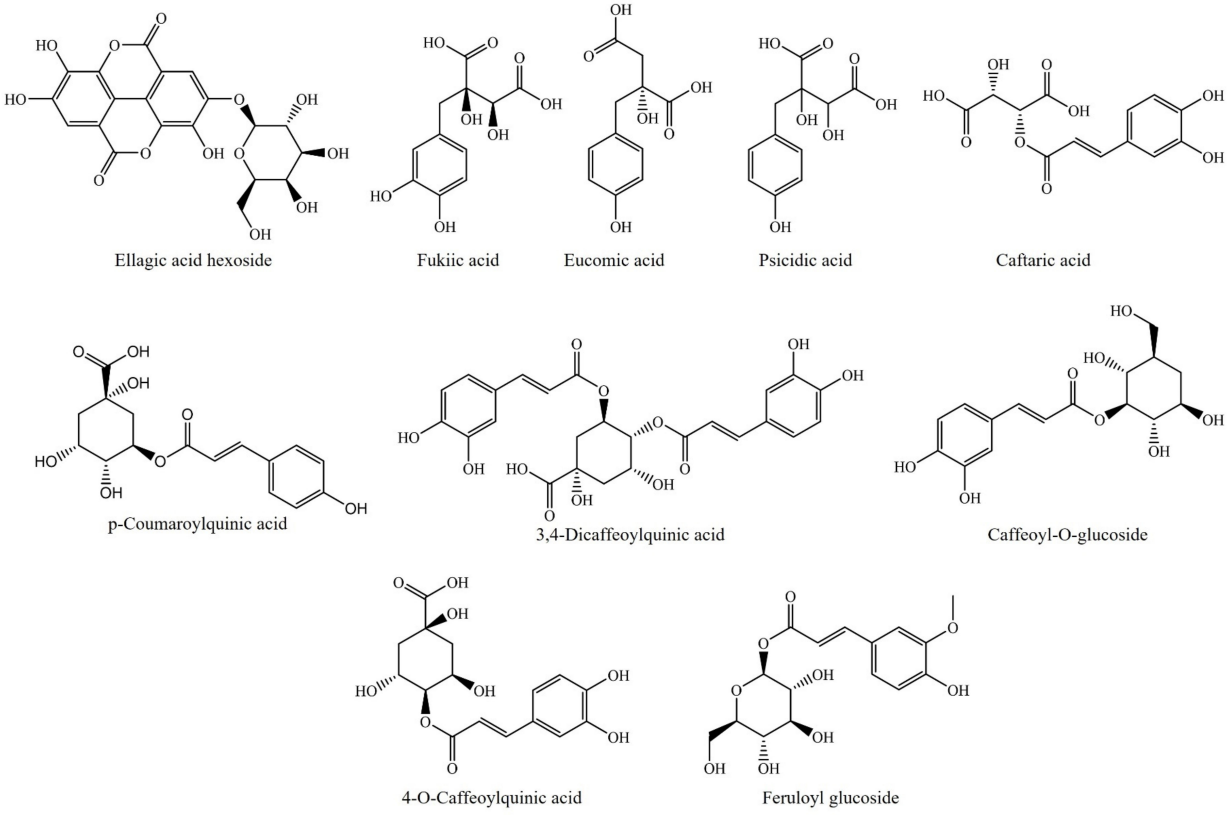
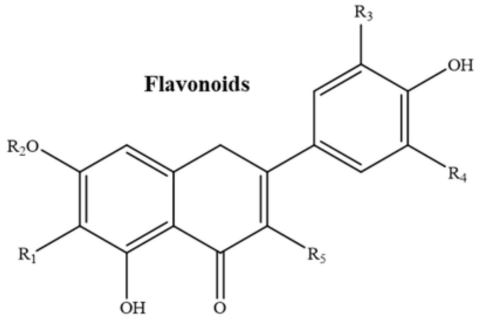


Figure 2. Current phenolic acids identified in the *Agave* genus.



	R_1	R_2	R_3	R_4	R_5	µg/g DW	Detection Method
Afzelin-3-O-gallate	H	H	H	H	O-GA	-	HPLC-MS/MS [29]
Apigenin	H	H	H	H	H	9.70	HPLC-UV-MS [29,30]
Apigenin-7-O-glucoside	H	O-glc	H	H	H	-	
Apigenin-7-O-rutinoside	H	O-rut	H	H	H	-	
Isorhamnetin-3-genthiotioside	H	H	OCH_3	H	O-gent	-	HPLC-MS/MS [29]
Isorhamnetin-3-O-rutinoside	H	H	OCH_3	H	O-rut	-	
Isorhamnetin-glucoside	H	H	OCH_3	H	O-glc	-	
Isorhmanetin	H	H	OCH_3	H	OH	1251.96 ±63.09	HPLC-UV-MS [29,30]
Kaempferol	H	H	H	H	OH	13.71	
Kaempferol 3-O-(caffeoyl)-sophoroside-7-O-glucoside	H	O-glc	H	H	O-CA-(soph)	16.68 ± 0.89	UHPLC-MS/MS [54]
Kaempferol 3-O-(feruloyl)-sophoroside-7-O-glucoside	H	O-glc	H	H	O-FA-(soph)	136 ± 5.3	
Kaempferol rhamnosido-malic acid	H	O-MA	H	H	O-rham	-	HPLC-MS/MS [29]
Kaempferol-3-O-(synapil)-sophoroside-7-O-glucoside	H	O-glc	H	H	O-SA-(soph)	363.4 ± 70	UHPLC-MS/MS [54]
Kaempferol-3-O-glucoside	H	H	H	H	O-glc	-	HPLC-MS [49]
Kaempferol-3-O-glucuronide	H	H	H	H	O-glc A	-	
Kaempferol-3-O-rutinoside	H	H	H	H	O-rut	265.3 ± 43	UHPLC-MS/MS [54]
Kaempferol-3-O-glucoside (Astragalin)	H	H	H	H	O-glc	-	HPLC-MS/MS [29,43]
Linarin	H	O-rut	H	OCH_3	H	-	
Luteolin	H	H	OH	H	H	-	HPLC-MS/MS [43]
Luteolin-3-O-rutinoside	H	H	OH	H	O-rut	238 ± 47.6	UHPLC-MS/MS [54]
Myricetin	H	H	OH	OH	OH	-	
Myricetin-3-O-rhamnoside	H	H	OH	OH	O-rham	-	HPLC-MS/MS [29]
Myricetin-O-gallate	H	H	OH	OH	O-GA	-	
Quercetin	H	H	OH	H	OH	15.57	HPLC-UV-MS [29,30] HPLC-MS [43]
Quercetin-3,7-O-dirhamnoside	H	O-rham	H	OH	O-rham	-	HPLC-MS/MS [29]
Quercetin-3-O-digalactoside	H	H	H	OH	O-gal	-	
Quercetin-3-O-feruloyl-7-O-sophoroside	H	O-glc	OH	H	O-FA-(soph)	18.55 ± 3.14	UHPLC-MS/MS [54] HPLC-MS [49]
Quercetin-3-O-glucoside	H	H	OH	H	O-glc	216.3 ± 40.3	UHPLC-MS/MS [54]
Quercetin-3-O-glucuronide	H	H	OH	H	O-glu A	754.1 ± 46	
Quercetin-3-O-rutinoside	H	H	OH	H	O-rut	-	HPLC-MS/MS [29]
Quercetin-3-O-sophoroside-7-O-glucoside	H	O-glc	OH	H	O-soph	21.99 ± 3.37	UHPLC-MS/MS [54]
Quercetin-3-O-xyloside	H	H	H	OH	O-xil	-	HPLC-MS/MS [29]
Quercetin-3-rutinoside-7-galactoside	H	O-gal	OH	H	O-rut	-	
Quercetin-O-di-p-coumaroyl-rhamnopyranoside	H	H	OH	H	O-(ACU)-rut	-	
Quercetin-sophoroside	H	H	OH	H	O-soph	43.05 ± 12.6	UHPLC-MS/MS [54]
Rutin	H	H	OH	H	O-rut	4027 ± 581	HPLC-MS/MS [43]

Figure 3. Current flavonoids identified and quantified in the Agave genus, glc = glucose; rut: rutinoside; gal = galactoside; rham = rhamnoside; soph = sophoroside; glu A = glucuronic acid; xil: xyloside; GA = gallic acid; gent = gentrobioside; SA = sinapic acid; FA = ferulic acid, ACU = cumaric acid; MA= mallic acid [29,30,43,49,54].

3.2. Non-Polar Compounds: Saponins

Saponins are a class of metabolites with both hydrophobic and hydrophilic properties. Their versatility as bioactive agents has been described through various bio-guided studies of the *Agave* species. From these plants, nearly 28 steroidal saponins and 86 glycosylated saponins have been isolated; however, these numbers are still increasing. These compounds have shown antifungal, anti-inflammatory, cytotoxic, anticancer, and hemolytic activities [65].

Santos-Zea et al. [55] investigated anticancer activity against pulmonary cancer cell-lines by applying enriched fractions of tetra and penta-glycosylated steroidal saponin from *A. salmiana* sap. The author found that the fraction that showed agavoside C and gentrogenin pentaglycoside contributed to cell death by necrosis at IC_{50}: 108.4 ± 11.5 µg/mL, while the fraction that presented magueyosides B, C, and kammogenin tetraglycoside induced apoptosis at IC_{50}: 82.7 ± 3.6 µg/mL. Such effects were similar to the anticancer

drug cisplatin which exerted necrosis and apoptosis at 10 µg/mL. Therefore, the anticancer activity of saponins depended on the glycosylated saponin derivative.

Furthermore, different fermented fractions of *A. sisalana* sap have been reported to exert anticancer activity but selectively through their different metabolic profiles. A fermented fraction from *A. globiformis* inhibited the growth of Caco-2 cell lines, while a *Gordonia* sp. fraction reduced Hep-G2 viability. Moreover, magueyoside B, and kammogenin glycoside were the most abundant in this extract and were associated with this bioactivity [57]. Another study showed that steroidal saponin, isolated from *A. marmorata* Roezl inhibited the NF-κB activation which modulates the inflammatory pathway of different diseases at IC_{50} of 0.01 µg/mL in RAW 264.7 macrophages [58].

The modulation of the neuroinflammatory response in rats was investigated by Herrera-Ruiz et al. [56] and it was reported that the leaf extracts of *A. tequilana* Weber and *A. americana* L. *marginata* Hort. at a dose of 125 mg/kg diminished TNF-α and IL-6 concentration levels compared to indomethacin at a dose of 5 mg/mL. In this research, cantala-saponin-1 was also isolated from an *A. americana* L. *marginata* Hort extract and it similarly decreased the concentration levels of these cytokines at 5 and 10 mg/kg of indomethacin. Alternatively, the administration of the extracts and the isolated saponin stimulated the production of the anti-inflammatory cytokine IL-10 [56]. Another study stated that the hydrolysate juice extract of *A. sisalana* Perrine did not exert mutagenic, cytotoxic, and neoplastic effects on Vero cells at a concentration of 50 mg/kg. At the same time, the positive control of cyclophosphamide showed clastogenic potential at the same dose [60]. Moreover, the hydrolysate extract reduced the levels of reactive oxygen species at 50 µg/mL. Interestingly, the author confirmed through HPLC-UV-vis a mixture of saponins with a variety of sugar moieties in hydrolysate extract [60]. Therefore, saponins could be safe and novel anti-neoplastic drugs compared to conventional chemotherapy agents.

Steroidal saponins have also showed gastroprotective activity. A recent study proved that isolated glycosylated steroidal saponin from *A. angustifolia marginata* did not produce hemolytic alterations in gastric tissue by the presence of different glycoside chain substitutions. This structural feature also reduced the affinity of cholesterol to the erythrocytes membrane and gave a cytoprotecting effect in these cells and non-cytotoxic damage [61]. Another study assessed the effect of a methanolic extract and a saponins-enriched fraction of *A. seemanniana* Jacobi leaves; both reduced ulcer severity in a similar way to ranitidine at 50 mg/kg. However, their effectiveness was at a concentration of 200 mg/kg [62]. The extracts also displayed anti-inflammatory and analgesic effects at a dose of 100 mg/kg. At this concentration, the therapeutic action was similar to aspirin (100 mg/kg) and indomethacin (20 mg/kg). In addition, the author confirmed through NMR the presence of glycosylated steroidal saponins in the active fractions [62].

The healing properties against ulcerative injuries in the rat colons were also investigated by applying extracts of *A. americana* Linn leaves. The effective dose of the extract was 200–400 mg/kg, and it reduced the catalytic activity of myeloperoxidase and lipoperoxidase, which are enzymatic markers involved in the inflammatory response of intestinal ulcerative colitis. After the application, the regeneration of the epithelial cells of the mucosa was observed. These healing effects were reached on the 11th day of application at a concentration of 400 mg/kg [66]. It is worth mentioning that at this concentration the extracts decreased the inflammation parameters such as colon length and weight more than acetic acid (4%) and indomethacin (7.5 mg/kg), which were used as positive controls in both studies. Besides, *A. americana* Linn leaves extracts had similar action to the standard drugs prednisolone and 1,3,3,3 tetra-ethoxy-propane used to treat this illness [66,67].

Steroidal glycosylated saponins were also identified in leaf extracts of *A. americana* var. *marginata*, *A. americana* L., *A. angustifolia* Haw cv. *marginata*, *A. desmettiana* Jacobi, and *A. pygmaea* Gentry, and the anti-inflammatory and ulceroprotective activities were attributed to these compounds, as well as fatty acid amides [51].

The study of the gastroprotective effect of isolated hecogenin of *A. sisalana* Perrine leaf was described on two ulcerative models, the ulcerative injuries were induced by ethanol

and indomethacin. Santos Cerqueira et al. [68] found that a dose of 90 mg/kg p.o. decreased the percentage of ulcerative injuries on the rats' stomachs, similar to commercial drugs such as ranitidine (100 mg/kg), *N*-acetylcysteine (300 mg/kg), and misoprostol in both ulcerative models. According to these findings, the author stated that hecogenin involved an antioxidant protector mechanism which consisted of the protection of thiol groups of non-protein molecules of gastric mucosa, antisecretory acid action, module inflammation, and through the regulated stimulation of prostaglandins biosynthesis. Additionally, the effective dose of hecogenin inhibited lipid peroxidation and myeloperoxidase release from neutrophils in the injury sites, which prevented the propagation of reactive oxygen species [68].

Overall, the obtention of natural products from agave agro-wastes might be advantageous in designing new therapies to treat gastrointestinal inflammatory diseases with novel antiulcerogenic agents.

Regarding the recovery of saponins, the assisted-ultrasound extraction was used on the bagasse of *A. salmiana*. The conditions that increased yields were 400-W, 24 kHz, and 60 °C. It is not recommended to use hydroalcoholic mixtures instead of water due to the low propagation of the ultrasound in those solvent systems [69]. Another technology employed on this agro-waste was supercritical fluid extraction assisted by an ultrasound. Increased antioxidant activity in the extracts was observed and the hexaglycosylated derivatives of hecogenin were identified among other steroidal saponins [70].

3.3. Phytosterols

Phytosterols are hydrophobic compounds, and their base structure is cholesterol. In plants, these metabolites do not occur in free form; rather, they can be presented as conjugates of esters, glycosides, and acyl groups [71].

A study using ultrasound-assisted extraction in the piña of *A. angustifolia* Haw. had high extraction yields of β-sitosterol-D-glycoside in short periods of the process compared to maceration extraction [72]. Hernández-Valle et al. [64] investigated the anti-inflammatory effect of acetone fractions of this species on a mice ear edema inflammation model induced by TPA. According to the authors, AaF16 was the most active fraction and decreased the levels of IL-1β, IL-6, and TNF-α at 0.8 mg/ear; this effect was greater than that of dexamethasone (0.1 mg/ear). Besides, the topic application of the fraction at this concentration showed minor mononuclear inflammatory cell infiltration than dexamethasone and TPA on skin and cartilage. The chemical profile obtained by NMR of the active fraction confirmed the presence of different phytosterols such as β-sitosteryl glycoside, stigmasterol, and a peracetylated derivative of 3-*O*-[6′-*O*-palmitoyl)-β-D-glucopyranosyl-sitosterol] [64], which are depicted in Figure 4.

Gutiérrez Nava et al. [63] compared the effect of the acetone extract of *A. tequilana* Weber leaf on rats with systemic erythematosus lupus (SLE) against methotrexate and prednisone, which are immunosuppressant and anti-inflammatory drugs used to treat this illness. The authors found that methotrexate (3 mg/kg) diminished the titer of DNA autoantibodies, but increased proteinuria levels; thus, it had a nephrotoxic effect. Conversely, *A. tequilana* Weber extracts reduced proteinuria associated with SLE, and decreased the titer of DNA autoantibodies, but not significantly. On the other hand, both drugs dropped the levels of IL-1β, IL-6, TNF-α, and INF-γ which are similar to the acetone fraction of *A. tequilana* Weber (50 mg/kg) which also stimulated the production of the IL-10 cytokine, a key cytokine that regulates the autoimmune response [63]. Through GC-MS, phytosterols and terpenes such as β-sitosterol-glycoside (0.1995), stigmasta-3,5-dien-7-one (0.0285), cycloartenol (0.019), and a phytol (0.1615) mg/g extract, were identified and quantified which were associated with this activity [63].

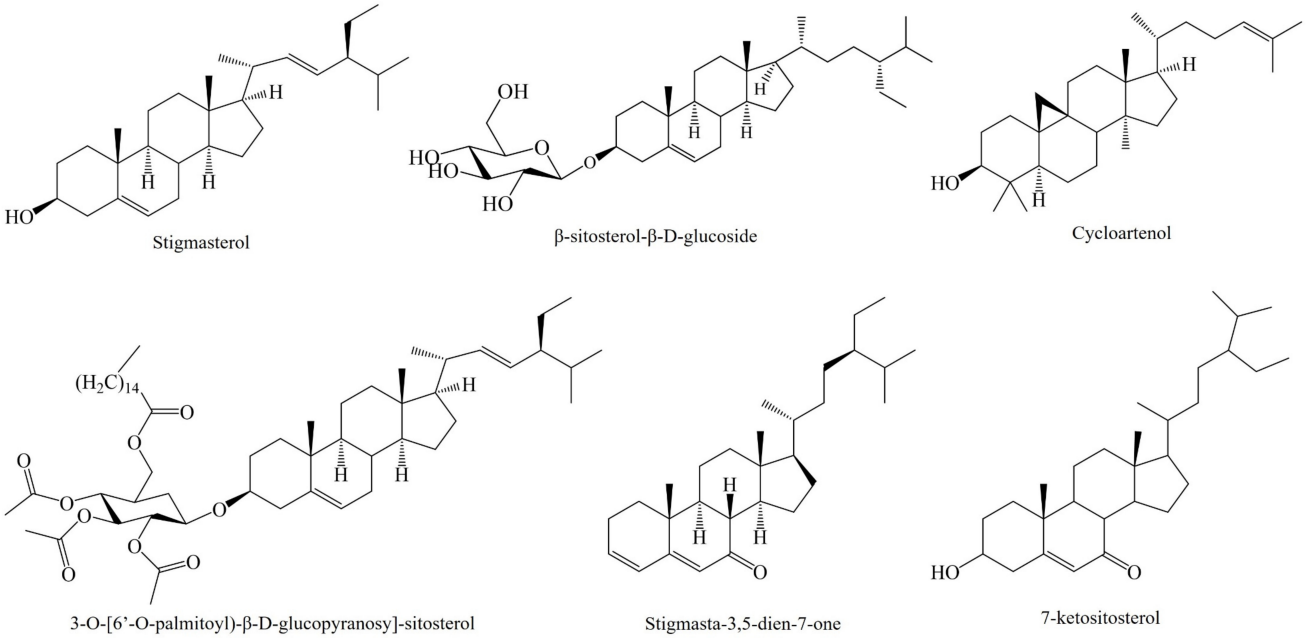


Figure 4. Current phytosterols identified and isolated in the *Agave* genus.

Furthermore, in the piña extracts from *A. angustifolia* Haw., *A. cupreata* Trel. & A. Berger, *A. salmiana* ssp. *Crassispina*, *A. salimiana* var. *salmiana*, *A. karwinskii* Zucc., leaf extracts of *A. atrovirens*, *A. decipiens* Baker, and a lipophilic fraction of fiber of *A. sisalana*, 7-ketositosterol, stigmasta-3,5-dien-7-one, stigmasta-4-en-3-one, stigmasta-4-en-3,6-dione and stigmastane-3,6-dione were found. However, no information was reported in this research about their biological activity [73–76].

4. The Role of *Agave* Extracts as Biopesticides

The application of agave crude extracts from agro-wastes has been on a diversity of applications on livestock and agricultural sectors. Since they are useful for pest insect management, larvae and intermedial organisms are considered vectors of parasitic diseases and fungi crop infestations.

4.1. Insecticide Activity

Lopes et al. [77] appraised the use of no contaminant solvents and applied a hydroalcoholic extract from *A. sisalana* Perrine leaf against adult females of *Dactylopius opuntiae*. The median lethal dose (LD_{50}) was 43 mg/mL after 10 h of application. Alternatively, the combination between extract and synthetic insecticide in their LD_{50} enhanced the mortality percentage because of the synergy between the insecticide compounds and extracts. This may be a strategy to introduce agave plants as biopesticides and diminish high concentrations of synthetic products in fields.

Guimarães de Oliveira et al. [78] observed that *A. sisalana* Perrine leaf juice had a cytotoxic effect on the hemocytes cells of *A. aegyptii* and increased at a dose of 6 mg/mL. As a result of the application of the extract, it incremented nitric oxide production, which stated a defense response against the secondary metabolites of the extract. On this agro-waste, saponins, triterpenoids, alkaloids, tannins, and flavonoids were detected by qualitative analysis and might be associated with this effect [79].

The leaf of *A. sisalana* Perrine has also been used for the biologic control of *Callosobruchus maculatus*. A concentration of 100 mg/mL reduced the oviposition, larvae survival and pupae stage, and their population on bean infested seeds [80].

The application of the leaf extract of *A. americana* var. *marginata* Trel. had a 70% mortality rate against *Brevicoryne brassicae* at a concentration of 0.75 mg/mL after 3 h of application [81]. Alternatively, this species activity showed 70.3% and 92% of mortality

against *Aphis gossypii* at 25 mg/mL after 24 and 36 h of application, respectively. However, the extract was toxic for *Artemisia salina*, a non-target organism [82].

Cunha Pereira et al. [83] identified β-caryophyllene in the aqueous extract of *A. americana* L. leaves as the most abundant compound, which had no deleterious effects in two species of bees; even at a high extract concentration, it showed CL_{50} of 127.4 and 122.2 ng/µL for *A. mellifera* y *P. helleri*, respectively. In contrast, imidacloprid had CL_{50} of 0.09 and 0.11 ng/µL in both species; therefore, the application of this pesticide resulted in more noxious effects than the extract. Moreover, Marafeli et al. [84] sprayed an aqueous extract of this species on coffee leaves infested with *Olygonychus ilicis* and it presented a 100% mortality rate at 4% (*v*/*v*) after 72 h of application.

Other species, such as *A. angustifolia* Haw., *A. tequilana* Weber, *A. sisalana* Perrine, and *A. attenuata* showed insecticide activity against *Bemicia tabaci*, *Tetranychus urticae*, and *Diuraphis noxia* [85–87]. Particularly, the extract of *A.attenuata* presented methyl-jasmonate, 2,5-dimethyl-3,4-hexanediol, and n-hexadecanoic acid as the most abundant metabolites, which might effect insecticide activity [88].

4.2. Molluscicide Activity

The agave crude extracts have been used for the biological control of mollusk. These organisms are vectors of diseases that affect human health due to are host of dangerous parasites.

From the above, different research has found that some *Agave* species such as *A. filifera*, *A. celsii*, *A. sisalana*, *A. decipiens* Baker, and *A. lophanta* exerted molluscicide activity against *Biomphalaria alexandrina* [75,89–91], a snail vector of *Schistosoma mansoni*, which causes schistosomiasis. The effective lethal dose and extract type are summarized in Table 3.

Table 3. Biopesticide potential of agave extracts.

Species/Tissue	Extract	Targeted Organism	Affected Organism	Biological Activity	LD_{50} (mg/mL)	MI (%)	t	References
A. americana L. Leaf	M	*Sitophilus oryzae* (L.)	*Triticum durum* Desf.	Insecticide Repellent	8.99 µg/cm^2 0.055 µg/cm^2	50	24 h	[49]
A. lechuguilla Torr. Leaf	HA	*Bemisia tabaci*	*Phaseolus vulgaris*	Insecticide	1035 mg/L	-	72 h	[50]
A. sisalana Perrine Leaf	HA	*Dactylopius opuntiae*	*Opuntia ficus-indica*	Insecticide	17, 46	51, 97	10 Days	[77]
A. sisalana Perrine Leaf juice	A	*Aedes aegyptii*	-	Ovicide Cytotoxic	6	73.8	24 h	[78]
A. sisalana Perrine Leaf	Hxn	*Callosobruchus maculatus*	*Phaseolus* spp.	Insecticide Ovicide	100	100	24–96 h	[80]
A. americana var. *Marginata* Trel. Leaf	A	*Brevicoryne brassicae*	*Brassica oleracea* L. var. *acephala*	Insecticide	0.750	>70	3 h	[81]
A. americana Leaf	A	*Aphis gossypii*	*Gossypium hirsitum* L.	Insecticide	25, 50	70.3, 92.5	24, 36 h	[82]
A. americana L. Leaf	A	*Olygonichus ilicis*	*Coffea arabica* L. *Coffea canephora*	Insecticide	4% (*v*/*v*)	100	72 h	[84]
A. angustifolia Haw. Leaf	A	*Tetranychus urticae*	*Fragaria* L. *Fragaria*	Insecticide	10% (*v*/*v*)	88	5 Days	[85]
A. tequilana Weber Leaf juice	Hxn	*Bemisia tabaci*	*Solanum lycopersicum*	Insecticide	20–40	90	24 h	[86]
A. sisalana Perrine Leaf juice	A	*Tetranycuhs urticae*	*Gossypium hirsitum* L.	Insecticide	-	100	35–65 Days	[87]
A. attenuata Leaf	A	*Dyuraphis noxia*	*Triticum* spp.	Insecticide	0.838	98.75	24 h	[88]
A. filifera *Whole plant*	A	*Biomphalaria alexandrina*	Humans	Molluscicide Ovicide	42.30 85.62	40.5	6 weeks	[89]
A. celsii Leaf	M	*Biomphalaria alexandrina*	Humans	Molluscicide	40, 73	-	24 h	[90]
A. lophantha Leaf	B	*Biomphalaria alexandrina*	Humans	Molluscicide	17, 100	100	48 h	[91]

Table 3. *Cont.*

Species/Tissue	Extract	Targeted Organism	Affected Organism	Biological Activity	LD_{50} (mg/mL)	MI (%)	t	References
A. attenuata Leaf	A	*Bulinus africanus*	Humans	Molluscicide	65	-	24 h	[92]
A. legrelliana Jacobi, *A. americana marginata* L. Leaf juice	A	*Praticolella griseola* (Pfeiffer)	Humans Animals Crops	Molluscicide	50% mL/L	82.5 77.5	7 Days	[93]
A. americana var. *expansa* Leaf	A	*Melanoides tuberculata* (Thiaridae)	Native mollusks Humans	Molluscicide	1.01 mL/L	65	24 h	[94]
A. americana Leaf	B	*Indoplanorbis exustus* *Lymnaea luteola* *Gyraulus convexiusculus*	Humans Animals	Molluscicide Ovicide	21.9, 18.5, 16 16.4, 15.2, 7.5	-	24 h	[95]
A. sisalana Perrine Leaf	A, B, E	*Pomacea canaliculata* L.	*Aegle marmelos*	Molluscicide	35.3 g/L, 93.3, 298.6	-	72 h	[96]
A. sisalana *A. attenuata* Leaf	E	*Biomphalaria alexandrina*	Humans	Molluscicide	82, 101	-	72 h	[97]
A. sisalana Perrine Leaf juice	A	*A. aegypti*	Humans	Larvicide	4.5, 6.5	100	12, 24 h	[98]
A. sisalana Perrine Leaf	A, M	*A. aegypti* *C. quinquefasciatus* *A. stephensi*	Humans	Larvicide	86, 76, 75 82, 220, 36	100	24 h	[99]
A. sisalana Leaf	A	*A. aegypti* *C. quinquefasciatus*	Humans	Larvicide	100	100	3–4 Days	[100]
A. cantala (Haw.) Roxb. Ex Salm-Dyck Leaf	Acn	*Plutella xylostella* (L.)	*Brassica oleracea*	Larvicide	60	35.77	12 h	[101]
A. sisalana Perrine Leaf juice	A	*Radopholus similis*	*Musa x paradisiaca*	Nematicide	5, 25% (*v*/*v*)	90.1, 99.2	24, 48 h	[102]
A. sislana Perrine Leaf juice	A	*Meloidogyne javanica*	*Solanum lycopersicum*	Nematicide	20% (*v*/*v*)	100	48 h	[103]
A. sisalana Perrine Leaf juice	A	*Scutellomena bradys*	*Dioscorea esculenta*	Nematicide	20–40% (*v*/*v*)	100		[104]
A. angustifolia Haw. Leaf	Acn	*Sitophilus zeamais* Motschulsky	*Zea mays* L.	Insecticide	5% (*v*/*v*)	34	72 h	[105]
A. angustifolia marginata Leaf	A	*A. aegypti* *C. quinquefasciatus* *A. stephensi*	Humans	Larvicide	28.27 µg/mL 100 µg/mL	100	12 h	[106]

HA: Hydroalcoholic, A: Aqueous, Hxn: n-Hexane, M: Methanolic, E: Ethanolic, Acn: Acetone, B: Butanol, MI %: Mortality index, DL_{50}: Median lethal dose, t: time.

Another study by Bakry and Salwa A.H [90] found that a dose of 22 mg/L of the methanolic leaf extract of *A. celsii* reduced the activity of the glycolytic enzymes of *B. alexandrina* and led the snails to an anoxia state. Alternatively, the extract administration caused the release of cellular content associated with the low enzyme activity of their energetic metabolism and diminished the oviposition rate, which prevented the propagation and infectivity of *S. mansoni* to *B. alexandrina.*

More studies have shown that the *A. legrelliana* Jacobi leaf juice extract exhibited molluscicide activity against *Praticolella griseola* with an 82.5% mortality rate after seven days [93]. Besides, this agro-waste was able to diminish notably the cardiac frequency of *Fossarium cubensis* within a range of 0.105 to 7.718 mL/L after three days of application [107].

Molluscicide activity of *A. americana* var. *expansa* was also assessed; the aqueous extract caused 65% of mortality against *Melanoides tuberculata* at LD_{50} of 0.86 mL/L after 24 h of exposition [94]. However, another study employed a butanol extract, and it showed an ovicide effect against *Indoplanorbis exutsus, Lymnaea luteola, and Gyraulus convexiusculus* at LD_{50} of 21.95, 18.56, and 16 mg/L, respectively [95].

The molluscicide activity of aqueous, ethanolic, and butanol extracts of *A. sisalana* Perrine leaf against *Pomacea canaliculate* was appraised. Particularly, aqueous extracts showed the highest molluscicide effect at LD_{50} of 35.3 mg/L [96]. Besides, the effective

concentration decreased superoxide dismutase activity due to the oxidative stress produced by the phytochemicals of the extract. Similarly, Hamed et al. [97] observed a modification in the activity of the antioxidant enzymes within the effective molluscicide concentration range. Thus, it might have involved a defense response brought about by secondary metabolites.

The molluscicidal activity of saponins was also investigated. A study showed that isolated tigogenin diglycoside from *A. angustifolia* leaves killed 90% of the *B. alexandrina* population at a concentration of 61.4 mg/L after 24 h of exposition [108]. Furthermore, in other research, steroidal glycosylated saponins from *A. franzosinii* P. Sewell and *A. angustifolia* exhibited this effect at LD_{50} similarly to niclosamide and praziquantel, which are synthetic molluscicides [109]. Moreover, neoruscogenin and neohecogenin isolated from *A. decipiens* Baker leaves had 90% mortality against this snail species at concentrations of 13 mg/mL and 6 mg/mL, respectively, after 24 h of application [75]. Considering this evidence, saponins might be an alternative to replace synthetic pesticides that might be noxious to the environment.

4.3. Larvicide Activity

Concerning larvicide activity, Kajla et al. [106] described that thermal stress on *A. angustifolia* var. *marginata* leaves swelled the concentrations of secondary metabolites in the extracts; this enhanced the mortality index against larvae *Aedes aegypti* at LD_{50} of 28.26 µg/mL after 12 h of application. Alternatively, the reduction in LD_{50} to 19.15 µg/mL was achieved, but during a longer exposition time (24 h). On the other hand, the extract also showed larvicide activity against *Culex quinquefasciatus* and *Anopheles stephensi*, but at 100 µg/mL.

Another study stated that the application of *A. sisalana* Perrine leaves juice killed *A. aegypti* larvae at LD_{50} of 4.5 mg/mL; the author reported that the high concentration of this agro-waste exhibited hemocytes necrosis and reduced nitric oxide concentration, which is involved in the immune response of this organism, after 24 h of application [98].

Furthermore, leaf juice extracts from *A. sisalana* Perrine obtained with water and other organic solvents were appraised. The aqueous extract killed *C. quinquefasciatus*, *A. aegypti*, and *A. stephensi* larvae at LD_{50} of 86, 76, and 75 mg/L, respectively. The highest mortality rate was on the III/IV growth stage of larvae. In contrast, the methanolic extract showed greater mortality at an LD_{50} of 36 mg/mL [99]; however, applying an organic solvent in plant molluscicides might represent an environmental risk. Moreover, Pizarro et al. [100] assessed the larvicidal effect of aqueous extracts of this species against *C. quinquefasciatus*, and it showed a mortality of larvae at LD_{50} of 322 mg/mL. In this research, the fractionation of crude extracts, was performed which enhanced the effect and reduced the LD_{50} to 204 mg/L, due to the increase in the saponins content and the elimination of undesirable compounds.

The larvicidal activity of *A. cantala* (Haw.) Roxb. Ex Salm-Dyck against *Plutella Xylostella* (L.) was weak at a 60 mg/L concentration with 35.77% mortality. However, a 25 mg/mL concentration prolonged the growth periods of the pupae and larvae, decreasing the fecundity rate of adult females and the hatching of the egg by 94.5% [101]. Thus, the disruption of reproductive cycles represents a strategy for plague control of other organisms that affect industrial crops.

4.4. Nematicide Activity

The field of bionematicides development through agave plants has gradually broadened as different research has proved the efficacy of agro-waste against different phytonematodes. Fábio et al. [102] observed that fresh leaf juice of *A. sisalana* Perrine exhibited 99.2% of mortality against *Radopholus similis* after 48 h, at 25% (*v*/*v*). In contrast, fermented juice at that concentration caused a phytotoxic effect on banana plants. Similarly, Damasceno et al. [103] found that the fresh juice of *A. sisalana* Perrine displayed 100% mortality on infested tomato crops with *Meloidogyne javanica* at 20% (*v*/*v*). In addition, the agro-waste

reduced nematode egg masses and the number of galls per plant. Conversely, fermented juice caused the inhibition of beneficial soil organisms. Likewise, Dos Santos Fernandes et al. [104] confirmed the nematicide activity of the liquid agro-waste of *A. sisalana* Perrine (20% *v*/*v*) against *Scutellomena bradys* with a 100% mortality rate after 24 h.

Another approach on the bionematicides from agave is the management of gastrointestinal nematodes in the livestock sector. Different *Agave* species such as *A. angustifolia* Haw., *A. americana* L., *A. tequilana* Weber and *A. sisalana* Perrine exhibited nematicide activity against *Panagrellus redivivus, Meloidogyne incognita, Haemonchus* spp., *Oesophagostomum* and *Trichostronglyus*. Those studies used methanolic and aqueous extracts, which killed nematodes within 24 to 72 h of application [86,110–112]. Another study mentioned that during the administration of *A. sisalana* Perrine agro-waste on infested animals, no health issues were presented. Thus, its application was considered safe [113].

As it mentioned previously, leaf juice of *A. sisalana* has been the most studied agro-waste for its nematicide properties. Hecogenin, succinic acid, mannitol, homoisoflavonoids, and kaempferol were some of the metabolites identified in aqueous sisal liquid agro-waste in different research [114,115].

4.5. Antifungal Activity

The use of extracts from agave agro-wastes as bioweapons against phytopathogenic fungus is another potential approach in agricultural areas. In general, *Postia placenta*, *Alternaria brassicae*, *Fussarum oxysporum*, *P. aphanidermatum*, *Phytophthora cinnamomi*, *Penicillium digitatum*, *Sclerotium rolfsii*, *Pyricularia oryzae* are fungi agents that are causing different plant diseases that affect industrial crops. However, different *Agave* species were efficient in their biologic control.

Some *Agave* species such as *A. americana* L., *A. sisalana* Perrine, *A. scabra* Salm-Dyck, *A. marginata*, *A. ferox* K. Koch, *A. lechuguilla* Torr., *A. montana* Villareal and *A. sisalana* Perrine inhibited mycelial hyphal growth or showed antisporulant effects against the previous fungi [116–121]. The effective concentration, extract type, type of inhibition, and affected crop were summarized in Table 4.

Table 4. Antifungal potential of agave extracts.

Species/Tissue	Extract	Target Organism	Affected Crop	Biological Activity	LD_{50}/MIC	IG (%)	t	References
A. montana Villareal *A. marginata* *A. americana* L. *A. ferox* K. Koch Leaf	AM	*Postia placenta*	-	Antifungal	-	69.31 [b]	7 days	[116]
A. americana L. Leaf	M	*Alternaria brassicae*	*Brassica juncea*	Antifungal	40 µg/mL	-	4 days	[117]
A. sisalana Perrine Leaf	A	*Pyricularia oryzae*	*Oryza sativa* L.	Antifungal	3% (*v*/*v*)	100 [a]	10 days	[118]
A. lechuguilla Torr. Leaf	A L	*Phytophthora cinnamomi*	*Persea americana Mill.*	Antifungal	28.87 23.07 mg/mL	60 [a]	-	[119]
A. americana L. Leaf	A	*Fusarium oxysporum* *Pythium aphanidermatum*	*Zingiber officinale* Rosc.	Antifungal	-	67.98 [a] 76.75 [a]	96 h	[120]
A. scabra, Salm Dyck Leaf	HA	*Botrytis cinerea* *Penicillium* sp.	-	Antifungal	-	90 [c] 86.6 [c]	7 days	[121]
A. americana L. Leaf	M	*Penicillium digitatum* *Sclerotium rolfsii*	-	Antifungal	11.86 21.97 µg/well	87.73 [a] 80.81 [a]	9 days	[122]
A. americana L. Leaf	M	*Sclerospora graminicola*	*Cenchrus americanus*	Antisporulant	-	-	12–14 h	[123]
A. lechuguilla Torr. Leaf	L C	*Rhizoctonia solani*	-	Antifungal	1.70×10^{4} [a] 6.72×10^{3} [a] mg/L	14.1 [c]	-	[124]
A. americana L. Leaf	A	*Aspergillus parasiticus*	*Cereal crops*	Reduce aflatoxin production	-	-	7 days	[125]

Table 4. *Cont.*

Species/Tissue	Extract	Target Organism	Affected Crop	Biological Activity	LD_{50}/MIC	IG (%)	t	References
- Leaf	E	*Penicillium* sp. *Penicillium variable* *Fusarium verticillioides*	*Phaseolus lunatus* L.	Antifungal	-	85 [c] 92.5 [c] 100 [c]	7 days	[126]
A. americana L. Leaf	A	*Phytophthora megakarya*	*Theobroma cacao* L.	Antifungal	60 mg/mL	54.33 [a]	7 days	[127]
A. sisalana Perrine Leaf juice	A	*Lasiodiplodia theobromae*	-	Antifungal		75.60 [a]	3 days	[128]
A. americana L. Leaf	-	*Leveillula taurica* (Lev.) Arn	*Capsicum annum* L.	Weak antifungal	-	-	10 days	[129]
A. cantala (Haw.) Roxb. Ex Salm-Dyck Leaf	A	*Peronospora farinosa*	*Vinis vinifera* L.	Fungal protection	-	-	10 days	[130]
A. marginata *A. americana* L. *A. ferox* K. Koch Leaf	AM	*Macrophomina phaseolina*	-	Antifungal	-	64.75 [b] 61.69 [b] 59.39 [b]	7 days	[131]
A. cantala (Haw.) Roxb. Ex Salm-Dyck Leaf	A	*Plasmopara viticola*	*Vinis vinifera* L.	Fungal protection	-	-	10 days	[132]
A. americana L. Leaf	A	*Sclerospora graminicola*	*Cenchrus americanus*	Antisporulant	-	-	12–14 h	[133]

LD_{50}: Median lethal dose, % IG: Inhibition growth percentage, MIC: Minimal inhibitory concentration, E: Ethanolic, M: Methanol, A: Aqueous, L: Lanolin, HA: Hydroalcoholic, AM: Aqueous methanol, C: Cocoa butter, [a]: Mycelial growth inhibition, [b]: Hyphal growth inhibition, [c]: Growth inhibition.

Maazoun, Hamdane, et al. [122] confirmed the antifungal effect of *A. americana* L. leaf extract against *P. digitatum*. Besides, the protease activity of this microorganism was inhibited at an IC_{50} concentration of 108.03 µg/mL. Another finding was that long exposition times of the extract to *P. digitatum* brought about the release of cell constituents which were correlated with the presence of saponins. On the other hand, the *A. americana* L. crude extract showed an antisporulant effect against *S. graminicola*. This effect was held after the extracts were diluted 10-fold. However, high diluted rates led to a lost antifungal effect [133].

The use of organic solvents such as methanol, n-hexane, and chloroform showed high antifungal activity [38,122]. Although, their application might be limited due to environmental issues. Castillo et al. [124] employed lanolin and cocoa butter instead of organic solvents on *A. lechuguilla* Torr. leaves with high tannin content. Additionally, these emulsions inhibited the mycelium growth of *R. solani* at concentrations of 1.70×10^4 and 6.72×10^3 mg/L, respectively. Similarly, Francisco et al. [119] confirmed the antifungal activity of lanolin extract of this species against *P. cinnamomi* at IC_{50} of 23.07 mg/mL. In contrast, lanolin extract exhibited an antifungal concentration lower than ethanolic extract but similarly to aqueous extract (28.87 mg/mL), which suggested that lanolin emulsions can also be efficient solvents to recover bioactive compounds.

The regulation of fungal disease of downy mildew on *vitis vinifera L* through *A. cantala* (Haw.) Roxb. Ex Salm-Dyck leaf extracts was investigated by Vishal Naik et al. [132]. It found that ten days of after the extract was sprayed, it stimulated the enzymatic activity of polyphenol oxidase and catalase. Such enzymes are involved in the production of reactive oxygen species and quinones, which act as a defense response against phytopathogenic fungi. On the same topic, another study reported that the leaf extract of *A. cantala* (Haw.) Roxb. Ex Salm-Dyck contained high polyphenolic content with radical scavenger capacity [134]. Thus, by the previous study, the content of phenolic compounds might play a key role in the regulation of fungi diseases.

The chemical nature of the secondary metabolites was a factor that influenced antifungal activity. Yang et al. [135] isolated different saponin glycosides from *A. americana* leaves and found that tigogenin tetraglycosides with one xylose unit enhanced this effect while

two or more xylose units decreased it. Therefore, the sugar chains impacted the antifungal potential of glycosylated steroidal saponins.

The agave crude extracts have also been referred to as excellent fungal toxin suppressors. Rosas-Taraco et al. [125] found that the aqueous extract of *A. americana* L. leaves decreased norsolorinic acid production by 75% at a concentration of 10 mg/mL. Norsolorinic acid is a precursor to the aflatoxin biosynthetic pathway. As a result of this, it reduced the aflatoxin concentration on *A. parasiticus*. Another study confirmed that aqueous extracts of *A. asperrima* Jacobi and *A. striata* Gentry inhibited 99% of the production of cyclopiazonic acid, a toxin biosynthesized by *A. flavus* on infested corn during storage [136]. Thus, agave extracts could have a useful application on cereal crop protection.

4.6. Antiparasitic Activity

There is little information about the potential of agave agro-waste extracts against parasites that are harmful to human health. At least two studies informed the antiparasitic activity against *Leishmania donovani*, the causal agent of visceral leishmaniasis.

According to the research of Singh et al. [137], the *A. americana* L. leaf extracts at 0.05 mg/L killed amastigotes and promastigotes of *L. donovani*, but this effect was preferably observed on amastigotes with 100% of mortality. Besides, the author compared the toxicity of extracts to amphotericin B, which resulted similarly to this commercial drug that is often used to treat visceral leishmaniasis. High costs, however, are a limitation in their treatment.

A second study reported that fractionated ethyl-acetate extracts from *A. americana* L. leaves obtained 100% mortality at 50 μg/mL against promastigotes and intracellular amastigotes of *L. donovani* at IC_{50} of 25 μg/mL. The application at effective doses increased nitric oxide levels in macrophages infested with amastigotes, which was suggested as a possible action mechanism of the extracts. However, after 48 h of dosing, a cytotoxic and hemolytic effect on macrophages was observed [138].

A third study reported by Quintanilla-Licea et al. [139] informed the antiparasitic activity of *A. lechuguilla* Torr. against *Entamoeba hystolytica*, the causal agent of amoebiasis, with a 69.66% growth inhibition; nevertheless, no median lethal dose was referred. More studies are required in this area, which offers a line of research to discover the antiparasitic effect of new molecules.

5. Conclusions

The hunting of novel bioactive molecules of the genus *Agave* and their biological activities shows that these plants are a valuable source of therapeutic agents, which can help generate new therapies for autoimmune, inflammatory, and chronic degenerative diseases. On the other hand, its use to obtain natural products might be a strategy to revalorize the agave agro-wastes, which could benefit the livestock and agricultural sectors due to the presence of secondary metabolites that play a protective role in bioweapons in pest control. Overall, natural extracts from agave agro-wastes might be an alternative for agricultural purposes because of their safety and low toxicity to the non-target organism compared to synthetic pesticides, which are harmful to the environment and human health. Being a material rich in different compounds of agro-industrial interest, future research focused on the isolation, purification, and protection of the secondary metabolites of the agave using environmentally friendly processes, as well as the latest sensitive and reliable technology instrumentation for their identification remain topics of interest for the use of agave agro-waste. On the other hand, delving into the development of products based on the use of these pure metabolites or its extracts, the evaluation of its stability and bioactivity, as well as its application in different areas of science will allow us to contribute to the circular economy of the production chain of the Agave.

Author Contributions: Conceptualization, M.E.-E. and J.E.U.-S.; writing—original draft preparation and collected bibliographic data, M.B.-B.; writing—review and editing, M.E.-E. and G.A.C.-H.; bibliographic and manuscript review, A.E.-R.; funding acquisition, M.E.-E. and G.A.C.-H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors are grateful to CONACYT (Council for Science and Technology of Mexico) for the scholarship granted to M.S. Bermúdez-Bazán M., and to CIATEJ, A.C. for the financial support provided for this publication.

Conflicts of Interest: The authors declare no conflict of interest.

Sample Availability: Samples of the compounds are not available from the authors.

References

1. Andrade, J.; De la Barrera, E.; Reyes, C.; Vargas-Soto, G.; Cervera, J. El Metabolismo Ácido de Las Crasuláceas: Diversidad, Fisiología Ambiental y Productividad. *Boletín Soc. Botánica México* **2007**, *81*, 37–50. [CrossRef]
2. García Mendoza, A. Distribution of Agave (Agavaceae) in Mexico. *Cact. Succul. J.* **2002**, *74*, 177–187.
3. García Mendoza, A.; Galván Villanueva, R. Riqueza de Las Familias Agavaceae y Nolinaceae En México. *Bot. Sci.* **2017**, 7. [CrossRef]
4. Gschaedler, A.C.; Gutiérrez Mora, A.; Contreras Ramos, S.M.; Davila Vazquez, G.; Gallardo Valdez, J. *Panorama del Aprovechaminto de Los Agaves en Mexico*; Gshchaedler Mathis, A.C., Villareal Hernández, S., Gutiérrez Mora, A., Ortiz Basurto, R.I., Moreno Terrazas Casildo, R., Lappe Oliveras, P.E., Larralde Corna, C.P., Contreras Ramos, S.M., Dávila Vázquez, G., Gallardo Váldez, J., Eds.; CONACYT, CIATEJ, AGARED: Guadalajara, Jalisco, Mexico, 2017; pp. 1–300, ISBN 9786079754853.
5. Pérez-Zavala, M.D.L.; Hernández-Arzaba, J.C.; Bideshi, D.K.; Barboza-Corona, J.E. Agave: A Natural Renewable Resource with Multiple Applications. *J. Sci. Food Agric.* **2020**, *100*, 5324–5333. [CrossRef]
6. Taylor, N.T.; Davis, K.M.; Abad, H.; McClung, M.R.; Moran, M.D. Ecosystem Services of the Big Bend Region of the Chihuahuan Desert. *Ecosyst. Serv.* **2017**, *27*, 48–57. [CrossRef]
7. Castillo Quiroz, D.; Cano Pineda, A.; Berlanga Retes, C. *Establecimiento y Aprovechamiento de Lechuguilla (Agave Lechuguilla Torr.)*; Comisión Nacional Forestal-Instituto Nacional de Investigaciones Forestales: Zapopan, México, 2012; pp. 1–33.
8. Díaz-Jiménez, L.; Carlos-Hernandez, S.; Jasso de Rodríguez, D.; Rodríguez-García, R. Conceptualization of a Biorefinery for Guishe Revalorization. *Ind. Crops Prod.* **2019**, *138*, 111441. [CrossRef]
9. Colunga-GarcíaMarín, P.; Torres-García, I.; Casas, A.; Figueredo-Urbina, C.J.; Rangel-Landa, S.; Delgado-Lemus, A.; Vargas, O.; Cabrera-Toledo, D.; Zizumbo-Villareal, D.; Aguirre-Dugua, X.; et al. Los Agaves y Las Prácticas Mesoamericanas de Aprovechamiento, Manejo y Domesticación. *Domest. Cont. Am.* **2017**, *2*, 273–309.
10. Radding, C. The Children of Mayahuel: Agaves, Human Cultures, and Desert Landscapes in Northern Mexico. *Environ. Hist. Durh. N. C.* **2011**, *17*, 84–115. [CrossRef]
11. Gentry, H.S. *Agaves of Continental North America*; University of Arizona Press: Arizona, North America, 1982; pp. 1–670, ISBN 9780816523955.
12. Davidson, J.R.; De Montellano, B.R.O. The Antibacterial Properties of an Aztec Wound Remedy. *J. Ethnopharmacol.* **1983**, *8*, 149–161. [CrossRef]
13. Irigoyen, F.; Paredes, A. *Tarahumara Medicine: Ethnobotany and Healing among the Raramuri of Mexico*; University of Oklahoma Press: Norman, OK, USA, 2015; pp. 1–416, ISBN 978-0-8061-4828-1.
14. Alinia-Ahandani, E.; Alizadeh, Z.; Sheydaei, M. Some Pointed Medicinal Plants to Treat the Tick-Borne Disease. *Open Access J. Bio. Sci. Res.* **2020**, *1*. [CrossRef]
15. Torre, L.D.L.; Cummins, I.; Logan-Hines, E. Agave Americana and Furcraea Andina: Key Species to Andean Cultures in Ecuador. *Bot. Sci.* **2018**, *96*, 246–266. [CrossRef]
16. Chaachouay, N.; Benkhnigue, O.; Zidane, L. Ethnobotanical Study Aimed at Investigating the Use of Medicinal Plants to Treat Nervous System Diseases in the Rif of Morocco. *J. Chiropr. Med.* **2020**, *19*, 70–81. [CrossRef]
17. García Mendoza, A.; Colunga-Garcia Marin, P.; Bye, R.J. Los Usos Del Agave Angustifolia Haw., Ancestro Silvestre Del Henequén En Su Área de Distribución Geográfica. *Boletín Soc. Botánica México* **1993**, *62*, 109–128. [CrossRef]
18. Delgado-Lemus, A.; Casas, A.; Téllez, O. Distribution, Abundance and Traditional Management of Agave Potatorumin the Tehuacán Valley, Mexico: Bases for Sustainable Use of Non-Timber Forest Products. *J. Ethnobiol. Ethnomed.* **2014**, *10*, 63. [CrossRef]
19. Ravikumar, S.; Venkatachalam, K.; Muruganandam, S. Ethnomedicinal Plants Used by the Malayali Tribals in Jawadhu Hills of Thiruvannamalai District, Tamil Nadu, India. *J. Nat. Prod. Plant Resour.* **2020**, *4*, 55–60.

20. Rahmatullah, M.; Pk, S.R.; Al-Imran, M.; Jahan, R. The Khasia Tribe of Sylhet District, Bangladesh, and Their Fast-Disappearing Knowledge of Medicinal Plants. *J. Altern. Complement. Med.* **2013**, *19*, 599–606. [CrossRef]
21. Phanuel, A.S. Plant Species in the Folk Medicine of Kit Mikayi Region, Western Kenya. *Ethnobot. Leafl.* **2010**, *2010*, 13.
22. Debnath, M.; Pandey, M.; Sharma, R.; Thankur, G.; Lal, P. Biotechnological Intervention of *Agave Sisalana*: A Unique Fibe Yielding Plant with Medicinal Property. *J. Med. Plant Res.* **2010**, *4*, 177–187.
23. Gidey, M.; Beyene, T.; Signorini, M.; Bruschi, P.; Yirga, G. Traditional Medicinal Plants Used by Kunama Ethnic Group in Northern Ethiopia. *J. Med. Plants Res.* **2015**, *9*, 494–509. [CrossRef]
24. Almaraz-Abarca, N.; Delgado-Alvarado, E.A.; Ávila-Reyes, J.A.; Uribe-Soto, J.N.; González-Valdez, L.S. The Phenols of the Genus Agave (Agavaceae). *J. Biomater. Nanobiotechnol.* **2013**, *4*, 33624. [CrossRef]
25. Rana, A.C.; Gulliya, B. Chemistry and Pharmacology of Flavonoids- A Review. *Indian J. Pharm. Educ. Res.* **2019**, *53*, 8–20. [CrossRef]
26. Alseekh, S.; Perez de Souza, L.; Benina, M.; Fernie, A.R. The Style and Substance of Plant Flavonoid Decoration; towards Defining Both Structure and Function. *Phytochemistry* **2020**, *174*. [CrossRef] [PubMed]
27. Barriada-Bernal, L.G.; Almaraz-Abarca, N.; Delgado-Alvarado, E.A.; Gallardo-Velázquez, T.; Ávila-Reyes, J.A.; Torres-Morán, M.I.; González-Elizondo, M.D.S.; Herrera-Arrieta, Y. Flavonoid Composition and Antioxidant Capacity of the Edible Flowers of *Agave Durangensis* (Agavaceae). *CYTA-J. Food* **2014**, *12*, 105–114. [CrossRef]
28. Almaraz-Abarca, N.; González-Elizondo, M.D.S.; Campos, M.D.G.; Ávila-Sevilla, Z.E.; Delgado-Alvarado, E.A.; Ávila-Reyes, J.A. Variabilidad de Los Perfiles Fenólicos Foliares Del Complejo Agave Victoriae-Reginae (Agavaceae). *Bot. Sci.* **2013**, *91*, 295–306. [CrossRef]
29. Morreeuw, Z.P.; Escobedo-Fregoso, C.; Ríos-González, L.J.; Castillo-Quiroz, D.; Reyes, A.G. Transcriptome-Based Metabolic Profiling of Flavonoids in *Agave Lechuguilla* Waste Biomass. *Plant Sci.* **2021**, *305*, 110748. [CrossRef] [PubMed]
30. Morreeuw, Z.P.; Castillo-Quiroz, D.; Ríos-González, L.J.; Martínez-Rincón, R.; Estrada, N.; Melchor-Martínez, E.M.; Iqbal, H.M.N.; Parra-Saldívar, R.; Reyes, A.G. High Throughput Profiling of Flavonoid Abundance in *Agave Lechuguilla* Residue-Valorizing under Explored Mexican Plant. *Plants* **2021**, *10*, 695. [CrossRef]
31. Puente-Garza, C.A.; Gutiérrez-Mora, A.; García-Lara, S. Micropropagation of *Agave Salmiana*: Means to Production of Antioxidant and Bioactive Principles. *Front. Plant Sci.* **2015**, *6*, 1–9. [CrossRef]
32. Puente-Garza, C.A.; Meza-Miranda, C.; Ochoa-Martínez, D.; García-Lara, S. Effect of in Vitro Drought Stress on Phenolic Acids, Flavonols, Saponins, and Antioxidant Activity in *Agave Salmiana*. *Plant Physiol. Biochem.* **2017**, *115*, 400–407. [CrossRef] [PubMed]
33. Morán-Velázquez, D.C.; Monribot-Villanueva, J.L.; Bourdon, M.; Tang, J.Z.; López-Rosas, I.; Maceda-López, L.F.; Villalpando-Aguilar, J.L.; Rodríguez-López, L.; Gauthier, A.; Trejo, L.; et al. Unravelling Chemical Composition of Agave Spines: News from *Agave Fourcroydes* Lem. *Plants* **2020**, *9*, 1642. [CrossRef]
34. Iser, M.; Valdivie, M.; Figueredo, L.; Nuñez, E.; Más Toro, D.; Martínez, Y. Secondary Metabolites, Quality Indicators and Organoleptic Characteristics of Stems Meal from *Agave Fourcroydes* (Henequen). *Cuba. J. Agric. Sci.* **2020**, *54*, 1–10.
35. Rahmani, H.; Benali, F.; Koudach, F.; Dif, M.M.; Mekhfi, N.; Nouredine, N.; Moumen, F.; Rahman, M. First Determination of Phenolic Compound Concentration and Antioxydant Activity of Agave Americana Leaves Extracts from Different Regions of Algeria (NW). *J. Med. Plant Res.* **2015**, *3*, 1–6.
36. Rahmani, H.; Toumi Benali, F. Phenolic Quantification and Antioxidant Activity of Agave Americana Leaves Depending on Solvent and Geoclimatic Area. *Adv. Environ. Biol.* **2016**, *9*, 194–200.
37. Ahumada-Santos, Y.P.; Montes-Avila, J.; de Jesús Uribe-Beltrán, M.; Díaz-Camacho, S.P.; López-Angulo, G.; Vega-Aviña, R.; López-Valenzuela, J.Á.; Heredia, J.B.; Delgado-Vargas, F. Chemical Characterization, Antioxidant and Antibacterial Activities of Six Agave Species from Sinaloa, Mexico. *Ind. Crops Prod.* **2013**, *49*, 143–149. [CrossRef]
38. Rizwan, K.; Zubair, M.; Rasool, N.; Riaz, M.; Zia-Ul-Haq, M.; de Feo, V. Phytochemical and Biological Studies of Agave Attenuata. *Int. J. Mol. Sci.* **2012**, *13*, 6440–6451. [CrossRef]
39. Delia, S.; Pérez-Herrera, A.; García-Sánchez, E.; Santiago Garcia, P. Identification and Quantification of Bioactive Compounds in *Agave Potatorum* Zucc. Leaves at Different Stages of Development and a Preliminary Biological Assay. *Waste Biomass Valorization* **2021**, *12*. [CrossRef]
40. Medina-Galván, M.I.; Bernardino-Nicanor, A.; Castro-Rosas, J.; De La Luz Xochilt Negrete-Rodríguez, M.; Conde-Barajas, E.; González-Cruz, L. Antimicrobial and Antioxidant Activity of Flower Scape Extracts of *Agave Salmiana*: Effect of the Extraction Solvent and Development Stage. *Res. J. Biotechnol.* **2018**, *13*, 1–9.
41. Ben Hamissa, A.M.; Seffen, M.; Aliakbarian, B.; Casazza, A.A.; Perego, P.; Converti, A. Phenolics Extraction from *Agave Americana* (L.) Leaves Using High-Temperature, High-Pressure Reactor. *Food Bioprod. Process.* **2012**, *90*, 17–21. [CrossRef]
42. López-Romero, J.C.; Ayala-Zavala, J.F.; Peña-Ramos, E.A.; Hernández, J.; González-Ríos, H. Antioxidant and Antimicrobial Activity of *Agave Angustifolia* Extract on Overall Quality and Shelf Life of Pork Patties Stored under Refrigeration. *J. Food Sci. Technol.* **2018**, *55*, 4413–4423. [CrossRef] [PubMed]
43. Contreras-Hernández, M.G.; Ochoa-Martínez, L.A.; Rutiaga-Quiñones, J.G.; Rocha-Guzmán, N.E.; Lara-Ceniceros, T.E.; Contreras-Esquivel, J.C.; Prado Barragán, L.A.; Rutiaga-Quiñones, O.M. Effect of Ultrasound Pre-Treatment on the Physicochemical Composition of Agave Durangensis Leaves and Potential Enzyme Production. *Bioresour. Technol.* **2018**, *249*, 439–446. [CrossRef] [PubMed]

44. Ameer, K.; Shahbaz, H.M.; Kwon, J.H. Green Extraction Methods for Polyphenols from Plant Matrices and Their Byproducts: A Review. *Compr. Rev. Food Sci. Food Saf.* **2017**, *16*, 295–315. [CrossRef]
45. Avila-Gaxiola, E.; Avila-Gaxiola, J.; Velarde-Escobar, O.; Ramos-Brito, F.; Atondo-Rubio, G.; Yee-Rendon, C. Effect of Drying Temperature on *Agave Tequilana* Leaves: A Pretreatment for Releasing Reducing Sugars for Biofuel Production. *J. Food Process Eng.* **2017**, *40*, 1–8. [CrossRef]
46. Santana-Jiménez, A.Z.; Quintero-Ramos, A.; Sánchez-Madrigal, M.Á.; Meléndez-Pizarro, C.O.; Valdez-Cárdenas, M.D.; Orizaga-Heredia, M.D.; Méndez-Zamora, G.; Talamás-Abbud, R. Effects of UV-C Irradiation and Thermal Processing on the Microbial and Physicochemical Properties of *Agave Tequilana* Weber Var. Azul Extracts at Various PH Values. *Processes* **2020**, *8*, 841. [CrossRef]
47. Anguiano-Sevilla, L.A.; Lugo-Cervantes, E.; Ordaz-Pichardo, C.; Rosas-Trigueros, J.L.; Jaramillo-Flores, M.E. Apoptosis Induction of *Agave Lechuguilla* Torrey Extract on Human Lung Adenocarcinoma Cells (SK-LU-1). *Int. J. Mol. Sci.* **2018**, *19*, 3765. [CrossRef] [PubMed]
48. Mitchell, V.D.; Taylor, C.M.; Bauer, S. Comprehensive Analysis of Monomeric Phenolics in Dilute Acid Plant Hydrolysates. *Bioenergy Res.* **2014**, *7*, 654–669. [CrossRef]
49. Maazoun, A.M.; Hamdi, S.H.; Belhadj, F.; Jemâa, J.M.; Messaoud, C.; Marzouki, M.N. Phytochemical Profile and Insecticidal Activity of Agave Americana Leaf Extract towards *Sitophilus Oryzae* (L.) (Coleoptera: Curculionidae). *Environ. Sci. Pollut. Res.* **2019**, *26*, 19468–19480. [CrossRef] [PubMed]
50. Ontiveros Guerra, J.G.; Chávez Cerna, E.; Ochoa Fuentes, Y.M.; Landeros Flores, J.; Aguirre Uribe, L.A.; Hernández Juárez, A. Insecticidal Activity of Plant Extracts against Whitefly Nymphs Bemisia Tabaci (Hemiptera: Aleyrodidae) in Laboratory. *J. Entomol. Zool. Stud.* **2020**, *8*, 595–599.
51. El-Hawary, S.S.; El-Kammar, H.A.; Farag, M.A.; Saleh, D.O.; El Dine, R.S. Metabolomic Profiling of Five Agave Leaf Taxa via UHPLC/PDA/ESI-MS Inrelation to Their Anti-Inflammatory, Immunomodulatory and Ulceroprotective Activities. *Steroids* **2020**, *160*, 108648. [CrossRef]
52. Sahnoun, M.; Saibi, W.; Brini, F.; Bejar, S. Apigenin Isolated from A. Americana Encodes Human and *Aspergillus Oryzae* S2 α-Amylase Inhibitions: Credible Approach for Antifungal and Antidiabetic Therapies. *J. Food Sci. Technol.* **2018**, *55*, 1489–1498. [CrossRef] [PubMed]
53. Sahnoun, M.; Bejar, S.; Daoud, L.; Ayadi, L.; Brini, F.; Saibi, W. Effect of *Agave Americana* L. on the Human, and Aspergillus Oryzae S2 α-Amylase Inhibitions. *Nat. Prod. Res.* **2019**, *33*, 755–758. [CrossRef]
54. Kyriacou, M.C.; El-Nakhel, C.; Pannico, A.; Graziani, G.; Soteriou, G.A.; Giordano, M.; Palladino, M.; Ritieni, A.; De Pascale, S.; Rouphael, Y. Phenolic Constitution, Phytochemical and Macronutrient Content in Three Species of Microgreens as Modulated by Natural Fiber and Synthetic Substrates. *Antioxidants* **2020**, *9*, 252. [CrossRef]
55. Santos-Zea, L.; Fajardo-Ramírez, O.R.; Romo-López, I.; Gutiérrez-Uribe, J.A. Fast Centrifugal Partition Chromatography Fractionation of Concentrated Agave (*Agave Salmiana*) Sap to Obtain Saponins with Apoptotic Effect on Colon Cancer Cells. *Plant Foods Hum. Nutr.* **2016**, *71*, 57–63. [CrossRef]
56. Herrera-Ruiz, M.; Jiménez-Ferrer, E.; Tortoriello, J.; Zamilpa, A.; Alegría-Herrera, E.; Jiménez-Aparicio, A.R.; Arenas-Ocampo, M.L.; Martínez-Duncker, I.; Monterrosas-Brisson, N. Anti-Neuroinflammatory Effect of Agaves and Cantalasaponin-1 in a Model of LPS-Induced Damage. *Nat. Prod. Res.* **2021**, *35*, 884–887. [CrossRef]
57. Figueroa, L.M.; Santos-Zea, L.; Escalante, A.; Gutiérrez-Uribe, J.A. Mass Spectrometry-Based Metabolomics of Agave Sap (*Agave Salmiana*) after Its Inoculation with Microorganisms Isolated from Agave Sap Concentrate Selected to Enhance Anticancer Activity. *Sustainability* **2017**, *9*, 2095. [CrossRef]
58. Cortés, A.J.; Sánchez-Mendoza, E.; Zamilpa, A.; González-Cortazar, M.; Herrera-Ruiz, M.; Almanza-Pérez, J.C.; Terán-Cabanillas, E.; Condé, R.; Domínguez-Ramírez, L.; Arcos, E.M.; et al. Steroidal Saponin from Agave Marmorata Roezl Modulates Inflammatory Response by Inhibiting NF-KB and AP-1. *Nat. Prod. Res.* **2020**, 1–6. [CrossRef] [PubMed]
59. De Oliveira, J.V.A.; Botura, M.B.; dos Santos, J.D.G.; Argolo, D.S.; da Silva, V.D.A.; da Silva, G.D.; de Lima, H.G.; Braz Filho, R.; Vieira, I.J.C.; Branco, A.; et al. Saponin-Rich Fraction from *Agave Sisalana*: Effect against Malignant Astrocytic Cells and Its Chemical Characterisation by ESI-MS/MS. *Nat. Prod. Res.* **2018**, *33*, 1769–1772. [CrossRef] [PubMed]
60. Araldi, R.P.; dos Santos, M.O.; Barbon, F.F.; Manjerona, B.A.; Meirelles, B.R.; de Oliva Neto, P.; da Silva, P.I.; dos Santos, L.; Camargo, I.C.C.; de Souza, E.B. Analysis of Antioxidant, Cytotoxic and Mutagenic Potential of *Agave Sisalana* Perrine Extracts Using Vero Cells, Human Lymphocytes and Mice Polychromatic Erythrocytes. *Biomed. Pharmacother.* **2018**, *98*, 873–885. [CrossRef]
61. Pereira, G.M.; Ribeiro, M.G.; da Silva, B.P.; Parente, J.P. Structural Characterization of a New Steroidal Saponin from *Agave angustifolia* Var. Marginata and a Preliminary Investigation of Its in Vivo Antiulcerogenic Activity and in Vitro Membrane Permeability Property. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 4345–4349. [CrossRef]
62. Mina, S.; Melek, F.R.; Abdel-Khalik, S.M.; El-Shaarawy, F.S.; Eskander, J. Pharmacological Activities of *Agave Seemanniana* and Isolation of Three Steroidal Saponins. *Eur. J. Med. Plants* **2014**, *4*, 271–283. [CrossRef]
63. Gutiérrez Nava, Z.J.; Jiménez-Aparicio, A.R.; Herrera-Ruiz, M.L.; Jiménez-Ferrer, E. Immunomodulatory Effect of *Agave Tequilana* Evaluated on an Autoimmunity Like-SLE Model Induced in Balb/c Mice with Pristane. *Molecules* **2017**, *22*, 848. [CrossRef]
64. Hernández-Valle, E.; Herrera-Ruiz, M.; Salgado, G.R.; Zamilpa, A.; Ocampo, M.L.A.; Aparicio, A.J.; Tortoriello, J.; Jiménez-Ferrer, E. Anti-Inflammatory Effect of 3-*O*-[(6′-*O*-Palmitoyl)-β-D-Glucopyranosyl Sitosterol] from *Agave Angustifolia* on Ear Edema in Mice. *Molecules* **2014**, *19*, 15624–15637. [CrossRef] [PubMed]

65. Sidana, J.; Singh, B.; Sharma, O.P. Saponins of Agave: Chemistry and Bioactivity. *Phytochemistry* **2016**, *130*, 22–46. [CrossRef] [PubMed]
66. Mannasaheb, B.; Kulkarni, P.; Sangreskopp, M.; Savant, C.; Mohan, A. Protective Effect of *Agave Americana* Linn. Leaf Extract in Acetic Acid-Induced Ulcerative Colitis in Rats. *Int. Q. J. Res. Ayurveda* **2015**, *36*, 101. [CrossRef] [PubMed]
67. Mannasaheb, B.; Kulkarni, V.; Shaikh, I.; Sangreskopp, M.; Savant, C. Gastro Protective Effect of Agave Americana Linn. Leaf Extract in Indomethacin-Induced Enterocolitis in Rats. *Int. J. Green Pharm.* **2015**, *9*, 229–235.
68. Santos Cerqueira, G.; Dos Santos E Silva, G.; Rios Vasconcelos, E.; Fragoso De Freitas, A.P.; Arcanjo Moura, B.; Silveira MacEdo, D.; Lopes Souto, A.; Barbosa Filho, J.M.; De Almeida Leal, L.K.; De Castro Brito, G.A.; et al. Effects of Hecogenin and Its Possible Mechanism of Action on Experimental Models of Gastric Ulcer in Mice. *Eur. J. Pharmacol.* **2012**, *683*, 260–269. [CrossRef]
69. Santos-Zea, L.; Gutierrez-Uribe, J.A.; Benedito, J. Effect of Solvent Composition on Ultrasound-Generated Intensity and Its Influence on the Ultrasonically Assisted Extraction of Bioactives from *Agave Bagasse* (*Agave Salmiana*). *Food Eng. Rev.* **2020**. [CrossRef]
70. Santos-Zea, L.; Gutiérrez-Uribe, J.A.; Benedito, J. Effect of Ultrasound Intensification on the Supercritical Fluid Extraction of Phytochemicals from Agave Salmiana Bagasse. *J. Supercrit. Fluids* **2019**, *144*, 98–107. [CrossRef]
71. Ferrer, A.; Altabella, T.; Arró, M.; Boronat, A. Emerging Roles for Conjugated Sterols in Plants. *Prog. Lipid Res.* **2017**, *67*, 27–37. [CrossRef]
72. López-Salazar, H.; Camacho-Díaz, B.H.; Ávila-Reyes, S.V.; Pérez-García, M.D.; González-Cortazar, M.; Arenas Ocampo, M.L.; Jiménez-Aparicio, A.R. Identification and Quantification of β-Sitosterol β-d-Glucoside of an Ethanolic Extract Obtained by Microwave-Assisted Extraction from *Agave Angustifolia* Haw. *Molecules* **2019**, *24*, 3926. [CrossRef]
73. Olvera-García, V.; Martín del Campo, S.T.; Gutiérrez-Uribe, J.A.; Cardador-Martínez, A. GC-MS and HPLC-MS-TOF Characterization of *Agave Atrovirens* Extracts. A Preliminary Study. *Ind. Crops Prod.* **2015**, *78*, 39–47. [CrossRef]
74. Martínez-Aguilar, J.F.; Peña-Álvarez, A. Characterization of Five Typical Agave Plants Used to Produce Mezcal through Their Simple Lipid Composition Analysis by Gas Chromatography. *J. Agric. Food Chem.* **2009**, *57*, 1933–1939. [CrossRef] [PubMed]
75. Abdel-Gawad, M.M.; El-Sayed, M.M.; Abdel-Hameed, E.S. Molluscicidal Steroidal Saponins and Lipid Content of *Agave Decipiens*. *Fitoterapia* **1999**, *70*, 371–381. [CrossRef]
76. Gutiérrez, A.; Rodríguez, I.M.; del Río, J.C. Chemical Composition of Lipophilic Extractives from Sisal (*Agave sisalana*) Fibers. *Ind. Crops Prod.* **2008**, *28*, 81–87. [CrossRef]
77. Lopes, R.S.; Oliveira, L.G.; Costa, A.F.; Correia, M.T.S.; Lima, E.A.L.-A.; Lima, V.L.M. Efficacy of Libidibia Ferrea Var. Ferrea and Agave Sisalana Extracts against *Dactylopius Opuntiae* (Hemiptera: Coccoidea). *J. Agric. Sci.* **2018**, *10*, 255. [CrossRef]
78. Guimarães de Oliveira, L.H.; Alexandria Paiva Silva de Sousa, P.; Felipe Hilario, F.; Joventino Nascimento, G.; Saraiva Morais, J.P.; Paulo de Medeiros, E.; Francisco de Sousa, M.; da Cruz Nunes, F. *Agave sisalana* Extract Induces Cell Death in Aedes Aegypti Hemocytes Increasing Nitric Oxide Production. *Asian Pac. J. Trop. Biomed.* **2016**, *6*, 396–399. [CrossRef]
79. Costa, M.F.; Tomás, J.; Osuna, A.; Brandão, H.N.; Haraguchi, M.; Alberto, C. Composição Química e Toxicidade Foliar de Extratos Do Resíduo Líquido de Sisal Chemical Composition and Foliar Toxicity of the Extracts from the Waste Liquid of Sisal Introdução Material e Métodos. *MAGISTRA* **2014**, *26*, 372–384.
80. Chrinius, H.; Musa, M.; Olalekan, B.A.; Usman Jajere, M.; Erphaim Akuaden, A.; Suleiman, B. Efficacy of Agave Sisalana N-Hexane Extract in the Control of *Callosobruchus maculatus* (Fabricius) (Colloptera: Bruchidae) Pest. *J. Appl. Biol. Biotechnol.* **2015**, *3*, 001–003. [CrossRef]
81. Pereira, A.J.; Cardoso, I.M.; Araújo, H.D.; Santana, F.C.; Carneiro, A.P.; Coelho, S.P.; Pereira, F.J. Control of *Brevicoryne Brassicae* (Hemiptera: Aphididade) with Extracts of *Agave americana* Var. Marginata Trel. in *Brassica oleracea* Crops. *Ann. Appl. Biol.* **2018**, 14–19. [CrossRef]
82. Fuertes, C.M.; Jurado, B.; Gordillo, G.C.; Negrón, L.P.; Núñez, E.; Esteban, M.; Távara, A. Estudio Integral de Plantas Biocidas Del Algodonero. *Cienc. Investig.* **2010**, *13*, 34–41. [CrossRef]
83. Cunha Pereira, R.; Faria Barbosa, W.; Pereira Lima, M.A.; Vieira, J.O.L.; Carvalho Guedes, R.N.; Rodrigues da Silva, B.K.; Dias Barbosa, G.M.; Lemes Fernandes, F. Toxicity of Botanical Extracts and Their Main Constituents on the Bees *Partamona helleri* and *Apis mellifera*. *Ecotoxicology* **2020**, *29*, 246–257. [CrossRef] [PubMed]
84. De Carvalho, T.M.B.; Reis, P.R.; de Oliveira, D.F.; Carvalho, G.A.; de Carvalho, D.A. Evaluation of Aqueous Extract of Plants for the Control of the Mite *Oligonychus ilicis* (McGregor, 1917) (Acari: Tetranychidae) on coffee tree. *Simpósio Pesqui. Cafés Bras.* **2009**, *3*, 94–103.
85. Veronez, B.; Sato, M.E.; Nicastro, R.L. Toxicidade de Compostos Sintéticos e Naturais Sobre Tetranychus Urticae e o Predador Phytoseiulus Macropilis. *Pesqui. Agropecu. Bras.* **2012**, *47*, 511–518. [CrossRef]
86. Herbert-Doctor, L.A.; Saavedra-Aguilar, M.; Villarreal, M.L.; Cardoso-Taketa, A.; Vite-Vallejo, O. Insecticidal and Nematicidal Effects of *Agave tequilana* Juice against Bemisia Tabaci and Panagrellus Redivivus. *Southwest. Entomol.* **2016**, *41*, 27–40. [CrossRef]
87. Barrêto, A.; Araújo, E.; Bonifácio, B. Eficiência de Extratos de *Agave sisalana* (Perrine) Sobre o Ácaro Rajado Tetranychus Urticae (Koch) e Ocorrência de Fitotoxidez Em Plantas de Algodoeiro (Gossypium Hirsutum L. r Latifolium Hutch). *Rev. Bras. Agroecol.* **2010**, *5*, 207–215.

88. Marieta, C.; Saba, L. The Impact of *Agave attenuata* Extracts: Biotic Resistance Esponses of Wheat and Their Ability to Act as Repellents/Insecticides against the Russian Wheat Aphid. *J. Plant Physiol. Pathol.* **2019**, *7*. [CrossRef]
89. Rawi, S.M.; Al-Hazmi, M.; Al Nassr, F.S. Comparative Study of the Molluscicidal Activity of Some Plant Extracts on the Snail Vector of *Schistosoma mansoni*, *Biomphalaria alexandrina*. *Int. J. Zool. Res.* **2011**, *7*, 169–189. [CrossRef]
90. Bakry, F.A.; Hamdi, S.A. The Molluscicidal Activity of Some Plant Extracts Against *Biomphalaria alexandrina* Snails. *Egypt. J. Exp. Biol.* **2006**, *2*, 99–106.
91. El-Sayed, M.M.; Abdel-Hadi, M.; El-Nahas, H.A. Molluscicidal Activity and Clinico-Pathological Effect of *Agave lophantha*. *Arch. Pharmal. Res.* **1991**, *14*, 81–86. [CrossRef] [PubMed]
92. Brackenbury, T.D. Gross Histopathological Effects of an Extract of Agave Attenuata on the Epithelium of the Digestive Tract of *Bulinus africanus*. *Ann. Trop. Med. Parasitol.* **1999**, *93*, 519–526. [CrossRef]
93. Nodarse, M.; Castellanos, L.; Herrera, N.; Morfa, M. Acción Molusquicida de Extractos Vegetales de Tres Especies de La Familia *Agavaceae* Contra *Praticolella griseola* (Pfeiffer). *Rev. Protección Veg.* **2017**, *32*.
94. Innacone, J.; La Torre, M.I.; Alvariño, L.; Cepeda, C.; Ayala, H.; Argota, G. Toxicity of the Biopesticides *Agave americana*, *Furcraea andina* (*Asparagacease*) and *Sapindus saponaria* (*Sapindaceae*) on Invader Snail *Melanoides tuberculata* (*Thiaridae*). *Neotrop. Helminthol.* **2013**, *7*, 231–241.
95. Sukumaran, D.; Parashar, B.D.; Rao, K.M. Molluscicidal Properties of *Agave americana* and *Balanites aegyptica*. *Int. J. Pharmacol.* **1994**, *32*, 232–238. [CrossRef]
96. Li, L.; Xu, W.-B.; Zhong, Q.-H.; Zhang, J.-E.; Luo, M.-Z.; Zhao, B.-L.; Qin, Z. Toxicological Effect of *Agave sisalana* Perrine Extract on Golden Apple Snail (*Pomacea Canaliculata* Lamarck). *Chin. J. Eco-Agric.* **2012**, *20*, 69–74. [CrossRef]
97. Hamed, R.R.; Maharem, T.M.; Farid, N.M.; Ramadan, K.; Abdel Aziz, M.H. Effect of *Agave attenuata* Extracts on Detoxification Enzymes of *Biomphlaria alexandrina*. *Environmentalist* **2006**, *26*, 157–164. [CrossRef]
98. Nunes, F.C.; Leite, J.A.; Oliveira, L.H.G.; Sousa, P.A.P.S.; Menezes, M.C.; Moraes, J.P.S.; Mascarenhas, S.R.; Braga, V.A. The Larvicidal Activity of *Agave sisalana* against L4 Larvae of Aedes Aegypti Is Mediated by Internal Necrosis and Inhibition of Nitric Oxide Production. *Parasitol. Res.* **2015**, *114*, 543–549. [CrossRef]
99. Singh, R.K.; Mittal, P.K.; Kumar, G.; Dhiman, R.C. Evaluation of *Mosquito larvicidal* Efficacy of Leaf Extract of a Cactus Plant, *Agave sisalana*. *J. Entomol. Zool. Stud.* **2014**, *2*, 83–86.
100. Pizarro, A.P.B.; Oliveira Filho, A.M.; Parente, J.P.; Melo, M.T.V.; Dos Santos, C.E.; Lima, P.R. O Aproveitamento Do Residuo Da Industria Do Sisal No Controle de Larvas de Mosquitos. *Rev. Soc. Bras. Med. Trop.* **1999**, *32*, 23–29. [CrossRef]
101. Reddy, G.V.P.; Urs, K.C.D. Growth Regulator Activity of the Xerophytic Perennial Plant, *Agave cantala* Roxb. on Diamondback Moth, *Plutella xylostella* (L.) (Lepidoptera: Yponomeutidae). *Int. J. Trop. Insect Sci.* **1991**, *12*, 439–442. [CrossRef]
102. Fábio, J.N.; Damasceno, J.C.A.; Barbosa, D.H.S.; Malheiro, R.; Pereira, J.A.; Soares, A.C.F. Control of the Banana Burrowing Nematode Using Sisal Extract. *Agron. Sustain. Dev.* **2015**, *35*, 783–791. [CrossRef]
103. Damasceno, J.C.; Soares, A.C.; Jesus, F.N.; Sant'Ana, R.S. Sisal Leaf Decortication Liquid Residue for Controlling *Meloidogyne javanica* in Tomato Plants. *Hortic. Bras.* **2015**, *33*, 155–162. [CrossRef]
104. Dos Santos Fernandes, J.; Silva Sousa, C.D.; Fermino Soares, A.C.; Sousa Lima, F.D.; Gomes Barbosa Silveira, D.H. Actinobacteria and Organic Fertilizer for Managment of the Nematode Scutellomena Bradys in Yam Plants. *Rev. Caatinga* **2016**, *29*, 548–558. [CrossRef]
105. Potenza, M.R.; Junior, J.J.; Alves, J.N. Evaluation of Contact Activities of Plant Extracts against *Sitophilus zeamais* Motschulsky (Coleoptera: Curculionidae). In Proceedings of the 9th International Working Conference on Stored-Product Protection, Campinas, São Paulo, Brazil, 15–18 October 2006; pp. 811–815.
106. Kajla, M.; Bhattacharya, K.; Gupta, K.; Banerjee, U.; Kakani, P.; Gupta, L.; Kumar, S. Identification of the Temperature Induced Larvicidal Efficacy of *Agave angustifolia* against Aedes, Culex, and Anopheles Larvae. *Front. Public Health* **2016**, *3*, 1–11. [CrossRef] [PubMed]
107. Yong, M.; Rodriguez, M. Evaluation of the Molluscicidal action of *Agave Legrelliana* on *Fossaria cubensis* (Molllusca: Lymnaeidae) Main Vecgtor of Fascioliasis in Cuba. *Parasitol. Día* **1994**, *18*, 46–49.
108. Abdel-Gawad, M.; El-Nahas, H.A.; Osman, N.S. Molluscicidal Activity of Steroidal Saponins Isolated from *Agave angustifolia*. *Glob. J. Pharmacol.* **2015**, *9*, 138–143. [CrossRef]
109. Mina, S.A.; Mina, S.A.; Melek, F.R.; Abdel-khalik, S.M.; Gabr, N.M. Two Steroidal Saponins from *Agave franzosinii* and *Agave angustifolia* Leaves and Biological Activities of *Agave franzosinii*. *J. Nat. Prod.* **2013**, *6*, 188–197.
110. Lubian, C.; Martinha, D.D.; Portz, R.; Gonçalves, M.P.; Holz, S.; Marcelino, W.L.; Nogueira, A.C.C.; Thomé, R.M.; Missio, V.C.; Cordeiro, J.; et al. Anthelmintic Activity of Plant Aqueous Extracts against *Panagrellus redivivus* in Vitro. *Arq. Inst. Biol.* **2019**, *86*, 1–11. [CrossRef]
111. Nandi, B. Evaluation of Nematicidal Properties and Inhibition of Egg Hatching Activity of Some Medicinal Plant Extracts Against Meloidogyne Incognita. *Res. Artic. NBU J. Anim. Sc* **2016**, *10*, 89–94.
112. Silveira, R.X.; Ana Carolina, S.; Mariana, B.; María José, M.; Luciana Morita, K.; Claudia María, L.; Alexsandro, M.; Elene de Alencar, A.; Simone, B.L.; María Angela, O.-A. Influência Do Resíduo Líquido Do Sisal (*Agave sisalana*, Perrine) Sobre a Alimentação Larvar. *Empres. Bras. Pesqui. Agropecuária* **2009**, 5–7.

113. Domingues, L.F.; Botura, M.B.; da Cruz, A.C.F.G.; Yuki, C.C.; da Silva, G.D.; Costa, M.S.; Murphy, G.; Moreira, E.L.T.; de Meneses, Í.D.S.; de Almeida, M.; et al. Evaluation of Anthelmintic Activity of Liquid Waste of *Agave sisalana* (Sisal) in Goats. *Rev. Bras. Parasitol. Vet.* **2010**, *19*, 270–272. [CrossRef] [PubMed]
114. Botura, M.B.; dos Santos, J.D.G.; da Silva, G.D.; de Lima, H.G.; de Oliveira, J.V.A.; de Almeida, M.A.O.; Batatinha, M.J.M.; Branco, A. In Vitro Ovicidal and Larvicidal Activity of *Agave sisalana* Perr. (Sisal) on Gastrointestinal Nematodes of Goats. *Vet. Parasitol.* **2013**, *192*, 211–217. [CrossRef]
115. Santos, J.D.G.; Vieira, I.J.C.; Braz-Filho, R.; Branco, A. Chemicals from Agave Sisalana Biomass: Isolation and Identification. *Int. J. Mol. Sci.* **2015**, *16*, 8761–8771. [CrossRef] [PubMed]
116. Siddhapura, S.; Maharshi, A.; Thaker, V. Varietal Difference in Antifungal Activity of Some Species of Agave. *Arch. Phytopathol. Plant Prot.* **2011**, *44*, 135–141. [CrossRef]
117. Guleria, S.; Kumar, A. Antifungal Activity of *Agave americana* Leaf Extract against Alternaria Brassicae, Causal Agent of Alternaria Blight of Indian Mustard (*Brassica juncea*). *Arch. Phytopathol. Plant Prot.* **2009**, *42*, 370–375. [CrossRef]
118. Kassankogno, A.; Ouedrogo, I.; Tiendrebeogo, A.; Ouedraogo, L.; Sankara, P. In Vitro Evaluation of the Effect of Aqueous Extracts of *Agave sisalana* and *Cymbopogon citratus* on Mycelial Growth and Conidia Production of *Pyricularia oryzae*, Causal Agent of Rice Blast. *J. Appl. Biosci.* **2015**, *89*, 8272. [CrossRef]
119. Castillo Reyes, F.; Hernández Castillo, F.D.; Julio Alberto, C.C.; Raúl, R.H.; Cristóbal Noé, A. In Vitro Antifungal Activity of Polyphenols-Rich Plant Extracts against *Phytophthora cinnamomi* Rands. *African J. Agric. Res.* **2015**, *10*, 4554–4560. [CrossRef]
120. Sharma, B.K. Antifungal Properties of Biocontrol Agents and Plants Extracts against Causal Fungi of Yellows and Rhizomes Rot of Ginger. *J. Biol. Control* **1998**, *12*, 77–80. [CrossRef]
121. González-Álvarez, M.; Moreno-Limón, S.; Salcedo-Martínez, S.M.; Pérez-Rodríguez, E.C. Evaluación in Vitro de La Actividad Antifúngica de Extractos de Agave (*Agave scabra*, Salm Dyck) Sobre Hongos Postcosecha. *Int. J. Exp. Bot.* **2015**, *84*, 427–434.
122. Maazoun, A.M.; Hamdane, A.M.; Mediouni, J.; Jemâa, B.; Marzouki, N. Saponin Content of *Agave americana* (L.) Leaf Extract and Its Antifungal Attributes against Phytopathogenic Fungi. *Int. J. Agric. Biosci.* **2019**, *8*, 106–111.
123. Adavigowda Deepak, S.; Oros, G.; Syagadadu Giriyanna, S.; Nandinin Pratap, S.; Huntrike Shekar, S.; Sheena, S. Antisporulant Activity of Leaf Extracts of Indian Plants against *Sclerospora graminicola* Causing Downy Mildew Disease of Pearl Millet. *Am. J. Agric. Biol. Sci.* **2004**, *38*, 31–39. [CrossRef]
124. Castillo, F.; Hernández, D.; Gallegos, G.; Mendez, M.; Rodríguez, R.; Reyes, A.; Aguilar, C.N. In Vitro Antifungal Activity of Plant Extracts Obtained with Alternative Organic Solvents against *Rhizoctonia solani* Kühn. *Ind. Crops Prod.* **2010**, *32*, 324–328. [CrossRef]
125. Rosas-Taraco, A.; Sanchez, E.; García, S.; Heredia, N.; Bhatnagar, D. Extracts of Agave Americana Inhibit Aflatoxin Production in *Aspergillus parasiticus*. *World Mycotoxin J.* **2010**, *4*, 37–42. [CrossRef]
126. De Oliveira Sousa, M.J.; de Almeida, F.A.; Leite, M.L.T.; Fonseca, W.L.; Lopes, K.P.; Gomes, C.D.L.; Sampaio, E.G.; da Nobrega Santos, E.; de Oliveira Gondim, A.R. Biocidal Potential of Some Organic By-Products on Sanitary and Physiological Quality of Red and White Fava Beans Seeds. *Aust. J. Crop Sci.* **2020**, *14*, 462–468. [CrossRef]
127. Bolanle Omofunmiloa, O. In vitro Antifungal Effects of Medicinal Plants Extraxt on the Mycelia Growth of *Phytophthora Megakarya* Causal Agent of Cocoa Blackpod Disease. *Pharm. Chem. Sci.* **2017**, *3*, 29–36.
128. Hong, H.X.; Fu, Y.H.; Xia, L.; Xiao, L.Z.; Hua, N.W.; Hui, L.; Xuan, Z. Antifungal Effects of Sisal Leaf Juice on *Lasiodiplodia theobromae*, the Causal Agent of Mulberry Root Rot. *African J. Biotechnol.* **2016**, *15*, 165–171. [CrossRef]
129. Hareesh, M.V.; Ganesha Naik, R.; Jayalakshmi, K.; Basavaraj Naik, T.; Pradeep, S. Efficacy of Bioagents, Plant Extracts and Fungicides against Chilli Powdery Mildew Incited by *Leveillula taurica* (Lev.) Arn. *J. Pure Appl. Microbiol.* **2016**, *10*, 3105–3109. [CrossRef]
130. Naik, V.V.; Bansode, M.S.; Bartakke, S.P. Foliar Application of Agave Cantala Roxb. Leaf Extract Enhances Antioxidative Defense Mechanism in Grape (*Vitis Vinifera* L.) Leaves Infected with Downy Mildew. *World J. Pharm. Res.* **2015**, *4*, 2039–2056.
131. Maharshi, A.R.; Thaker, V.S. Antifungal Activity of Agave Species from Gujarat, India. *Microb. Divers. Biotechnol. Food Secur.* **2014**, 423–430. [CrossRef]
132. Naik, V.; Bartakke, S. Effect of *Agave cantala* Leaf Extract on Downy Mildew of Grape. *BIOINFOLET Q. J. Life Sci.* **2009**, *6*, 249–250.
133. Adavigowda Deepak, S.; Oros, G.; Shekar Shetty, H.; Sheena, S. Antisporulant Activity of Watery Extracts of Plants against Sclerospora Graminicola Causing Downy Mildew Disease of Pearl Millet. *Am. J. Agric.* **2007**, *2*, 36–42. [CrossRef]
134. Koteswara Reddy, G.; Iakshmi Mohana, S.; Ashok Kumar, C.K.; Kumar Satheesh, D.; Lakshmi Srinivas, T. Evaluation of Anti-inflammatory and Antioxidant Activity of Methanolic of Agave cantala Roxb. *J. Glob. Trends Pharm. Sci.* **2013**, *4*, 1300–1309.
135. Yang, C.R.; Zhang, Y.; Jacob, M.R.; Khan, S.I.; Zhang, Y.J.; Li, X.C. Antifungal Activity of C-27 Steroidal Saponins. *Antimicrob. Agents Chemother.* **2006**, *50*, 1710–1714. [CrossRef] [PubMed]
136. Sánchez, E.; Heredia, N.; García, S. Inhibition of Growth and Mycotoxin Production of *Aspergillus flavus* and *Aspergillus parasiticus* by Extracts of Agave Species. *Int. J. Food Microbiol.* **2005**, *98*, 271–279. [CrossRef] [PubMed]
137. Singh, S.K.; Bimal, S.; Narayan, S.; Jee, C.; Bimal, D.; Das, P.; Bimal, R. Leishmania Donovani: Assessment of Leishmanicidal Effects of Herbal Extracts Obtained from Plants in the Visceral Leishmaniasis Endemic Area of Bihar, India. *Exp. Parasitol.* **2011**, *127*, 552–558. [CrossRef] [PubMed]

138. Thakur, C.P.; Narayan, S.; Bahadur, S.; Thakur, M.; Pandey, S.N.; Kumar, P.; Misra, P.; Mukherjee, P.K.; Mitra, D.K. Anti-Leishmanial Activity of *Agave americana* L.– A Traditional Indian Medicinal Plant. *Indian J. Tradit. Knowl.* **2015**, *14*, 658–663.
139. Quintanilla-Licea, R.; Mata-Cárdenas, B.D.; Vargas-Villarreal, J.; Bazaldúa-Rodríguez, A.F.; Ángeles-Hernández, I.K.; Garza-González, J.N.; Hernández-García, M.E. Antiprotozoal Activity against *Entamoeba histolytica* of Plants Used in Northeast Mexican Traditional Medicine. Bioactive Compounds from Lippia Graveolens and Ruta Chalepensis. *Molecules* **2014**, *19*, 21044–21065. [CrossRef] [PubMed]